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Foreword by the Editor

At the Seventh session of the Commission on Narcotic Drugs it was suggested by some representatives that the "Bulletin on Narcotics" should publish a special issue dealing with heroin. The editors now have the honour to present such a number. Several specialists in the field were invited to write articles for it but, in a few cases, it has been impossible to get the material ready for its publication in this issue; the editors are therefore already considering the advisability of preparing another issue on the subject of heroin, which would contain supplementary information, especially concerning the attitude of the World Health Organisation to the matter. Moreover, the bibliography, although quite comprehensive in this number, is far from being complete and could be added to.

History of Heroin

INTRODUCTION

The great advances in medical therapy in the past century have been due largely to the rapid development of chemistry and pharmacology. During this period innumerable compounds obtained in chemical laboratories, were tested for their pharmacological activity. Those proving satisfactory were then produced commercially.

The extent of public acceptance and usage of any one drug has usually been determined by the medical profession. The use of many of the new compounds was only of short duration; they were frequently replaced by other compounds found to be more effective, or which did not provoke inconvenient side reactions.

The case of "Heroin" (diacetylmorphine) is almost unique. Hailed as a wonder drug, it was received with enthusiasm by the medical profession. Inevitably, the deleterious effects of the drug were discovered. Although many doctors discontinued prescribing heroin and all warned against careless use of the drug, the market for it continued to flourish. A dangerous addiction-producing drug, it was not easy to curtail its usage.

This paper proposes to trace the story of heroin from its discovery and enthusiastic acceptance until its present doubtful status to-day.

HEROIN AS A WONDER DRUG

Although diacetylmorphine was not prescribed as a medicine much before 1900 its preparation had already been reported in 1874 by C. R. Wright at St. Mary's Hospital in London.[1] The main purpose of his work was to determine the constitution of some natural and purified alkaloids. By boiling anhydrous morphine alkaloid for several hours with acetic anhydride he was able to isolate acetylated morphine derivatives. The general conception of the morphine molecule in those days was that it was represented by the double empirical formula[2] which gave rise to the rather confusing nomenclature in his article. The extreme acetylated derivative which he obtained, he called "*Tetra acetyl* morphine." This compound corresponds to diacetylmorphine according to our present nomenclature.

This "Tetra acetyl morphine" was sent to F. M. Pierce, Associate at Owens College, London, for biological assay. After having tested the compound in *animal* experiments he reported the following results to Wright. The effects were:[1] "...great prostration, fear, sleepiness speedily following the administration, the eyes being sensitive and pupils dilated, considerable salivation being produced in dogs, and slight tendency to vomiting in some cases, but no actual emesis. Respiration was at first quickened, but subsequently reduced, and the heart's action was diminished and rendered irregular. Marked want of co-ordinating power over the muscular movements and the loss of power in the pelvis and hind limbs, together with a diminution of temperature in the rectum of about 4°, were the most noticeable effects."

From a medical point of view the interest in this new morphine derivative was not very high for the first twenty years. In 1890, a German scientist, W. Dankwortt,[3] prepared diacetylmorphine by heating anhydrous morphine with excess acetylchloride. The result of his work is important, not from the pharmacological, but from the chemical point of view. Because of the nature of the compounds he was able to isolate, he concluded that the morphine molecule had a simple empirical formula rather than the double one.

In the last decade of the 19th century Dreser[4] and other investigators studied the physiological effects of diacetylmorphine. The favourable reports of these investigators along with the growing interest in the drug shown by the medical profession of that time, led the Bayer Company in Eberfeld, Germany, to start production of the compound on a commercial scale (1898).

The new compound was marketed by Bayer under the name "Heroin." (The name is probably derived from "heroisch" which in German medical terminology means large, powerful, extreme, one with pronounced effect even in small doses.) Later this name became a synonym for the drug.

The new remedy received a spontaneous and widespread acceptance comparable to the acceptance of drugs like penicillin or cortisone in the past few years. The high frequency of tuberculosis and other respiratory diseases had created a great demand for an effective remedy and it was hoped that heroin would meet this need.

Prescribed for almost all illnesses in which codeine or morphine had been found, heroin was also considered to be effective in combating addiction to these two drugs. This enthusiasm for the new drug is best illustrated in the medical literature of the time. Though by no means exhaustive, these following excerpts are typical of the writings of the day.

In 1898, Strube[5] reported on the results of studies at the Medical University Clinic of Berlin. Testing heroin on 50 patients afflicted with phthisis, he found it effective in relieving their cough and in producing sleep. Though Strube observed no adverse effects, he

Farbenfabriken
прежде
Friedr. Bayer & Co
Elberfeld.
Фармацевтический отдѣлъ.
ASPIRIN
Antirheumaticum
HEROIN
LOPHEN
CREOSOTAL
DUOTAL
Представители ФРИДР. БАЙЕРЪ и К°. въ С.-Петербургѣ и въ Москвѣ.

Farbenfabriken vorm. Friedr. Bayer & Co., Elberfeld.
Abteilung für pharmaceutische Produkte
Tannopin
Heroin
hydrochloric.
Aristol
Eisen-
Somatose
(Ferro-Somatose)
Trional
Sicheres
Hypnoticum.
Jodothyrin
Creosotal
Aspirin
(Acetylsalicylsäure)

DISSOLVE ON THE TONGUE
Antikamnia & Heroin
Tablets
(5 GR. ANTIKAMNIA, 1/12 GR. HEROIN HYDROCHLOR.)
A RESPIRATORY STIMULANT, SEDATIVE, EXPECTORANT AND ANALGESIC
IN THE TREATMENT OF
COUGHS, BRONCHITIS, LARYNGITIS, PNEUMONIA, DYSPNŒA, PHTHISIS, CORYZA, WHOOPING COUGH, ASTHMA, HAY FEVER, COLDS, ETC.
DOSE: ONE TABLET EVERY TWO, THREE OR FOUR HOURS AS INDICATED
SAMPLE BOX FREE TO PHYSICIANS
ADDRESS
CHEMICAL COMPANY - St. Louis, U.S.A.

Farbenfabriken vorm FRIEDR. BAYER & Co., ELBERFELD.

Salofene

Neuralgie, emicranie e cefalalgie.

Dose: 1 gr. da ripetersi dopo 1/2 ora in caso di bisogno.

Reumatismo articolare acuto, Corea, Sciatica ed influenza.

Dose: 1 gr. 4 a 6 volte al giorno.

Riparto prodotti farmaceutici

Marca di Fabbrica

Agurina

(Teobromin - Sodio acetico)

Diuretico attivissimo

Dose: da gr. 0,5 a gr. 1,0 fino a raggiungere in totale 3 gr. al giorno.

Somatose

ALBUMINOIDI DELLA CARNE (ALBUMOSI).

Polvere insipida, intieramente solubile. Ricostituente di prim'ordine indicato nella convalescenza dalle affezioni ipostenizzanti, perdite di sangue, operazioni gravi, nella anemia delle puerpere, nella tisi, rachitismo, ecc.

Edonale

Nuovo ipnotico

Assolutamente innocuo, privo di effetti secondari.

Dose: 1 1/2 - 2 gr. in polvere, esclusivamente in ostie. Anche per clisma.

Eurofene

Succedaneo dell'iodoformio, impiegato nella bassa chirurgia.

Specifico nell'ulcera molle, piaghe sifilitiche.

Puro o mescolato per metà con acido borico perfettamente od unguento al 5 a 10 %.

Cloridrato d' Eroina

Facilmente solubile nell'acqua, adatto per somministrarsi a gocce e in miscugli.

Surrogato della morfina per uso sottrattivo.

Dosi per uso interno: Per adulti: 0,008-0,005 gr. da 3 a 4 volte al giorno (dose giornaliera complessiva 0,08 gr.) — Per bambini: 0,0005-0,0025 gr. da 3 a 4 volte al giorno.

Dosi per iniezioni sottocutanee: gr. 0,008-0,005-0,01.

☞ Si raccomanda di ridurre la prima iniezione a metà delle dosi suddette.

Protargolo

Un nuovo preparato organico d'argento per la cura della Gonorrea (distruzione dei gonococchi) per la cura delle ferite. Oftalmia.

Sterilizzabile, proprietà battericide senza irritare.

Solub. in casi di Gonorrea 1 a 2 %. — Solub. in casi di Oftalmia 10 a 20 %. — *Unguento.*

Deposito generale per l'ITALIA

e C.ia

15, Via

MILANO.

Letteratura ai Signori Medici

Aspirina

Nuovo succedaneo dei salicilati. Etere acetico dell'Acido salicilico; senza agradevoli effetti secondari; attraversa lo stomaco senza decomporsi; si sdoppia nei suoi elementi solo in presenza dell'alcalinità del succo intestin.

Dose: 1 gr. (con 3 a 4 gr. di zucchero in 15 gr. d'acqua) 3 a 4 volte al giorno.

Farbenfabriken vorm. Friedr. Bayer & Co., Elberfeld.

Pharm. Abteilg.

Salochinin

(Salicylester des Chinins)

Vollkommen geschmackfreies Antipyreticum und Analgeticum. Ind.: fieberhafte Zustände, besond. typhöse Fieber, Malaria. — Neurosen (Neuralgieen, Ischias).

Dos.: 1 - 2 g. ein- oder mehrmals täglich.

Rheumatin

(salicylsaurer Chininsalicylester)

Antirheumaticum.

Ind.: akut. Gelenkrheumatismus, namentl. bei empfindlichen und schwachen Fällen

Dos.: 4 g. pro die.

Agurin

Essigsaures Theobromin-natrium.

Neues Diureticum.

Dos.: 0,5—1 g: pro die 3 g.

Aspirin

Antirheumaticum u. Analgeticum.

Bester Ersatz für Salicylate. Angenehm säuerlich schmeckend; nahezu frei v. all. Nebenwirkungen.

Dos.: 1 g. 3—5 mal täglich.

Heroin. hydrochl.

vorzügliches Sedativum bei allen Erkrankungen d. Luftwege. Ersatz für Morphin und Codein. Leicht wasserlöslich, reizlos.

Dos.: Erwachs. 0,010—0,015 g. 3—4 mal täglich.

Kinder 0,005—0,005 g 3—4 mal täglich.

Nedonal

Neues Hypnoticum.

Absolut unschädlich, frei von Nebenwirkungen.

Spez. Ind.: nervöse Agrypnie (bes. bei Depressionszuständen etc.)

Dos.: 1,5—2 g. als Pulver, ev. in Oblaten; auch per clysma.

Salophen — Creosotal — Duotal — Protargol — Aristol — Tannigen — Trional — Somatose — Eisen-Somatose.

felt that further observations were necessary to determine whether continual use might be harmful or lead to chronic "heroinism."

At the request of Dreser, Floret experimented with the drug in the Poliklinik der Farbenfabriken (1898).[6] He found it valuable in the treatment of bronchitis, asthma and tuberculosis. For cases of dry bronchitis where codeine has been ineffective, Floret reported that heroin was unusually prompt and dependable.

These were among the experiments that led to Dreser's[7] endorsement of heroin at the congress of German Naturalists and Physicians in 1898. Claiming that heroin was ten times as effective as codeine in the treatment of respiratory diseases, he estimated that it had only one-tenth of the toxic effects.

H. Leo[8] in reporting the frequent success he had observed in administering the drug, gave a detailed case history of one of his patients. In 1896, the patient, then 71 years of age, developed a severe cough with expectoration and suffered from dyspnea. After being hospitalized in the summer of 1897, and again in the summer of 1898, the patient was finally sent to a sanatorium in November 1898. By this time his condition had become considerably worse. Respiration was rapid and difficult, fat and muscular tissue had deteriorated, the lungs were enlarged and heart action was poor.

By February 1899, drugs no longer afforded the patient any relief and he was unable to sleep at night. Heroin was then prescribed. The description of the treatment follows:

> "February 4. The patient had been given the first dose the evening before. The night was still without sleep, but the cough was looser and effortless. Also the dyspnea was not so pronounced. After he had taken the drug he felt very comfortable and stated that he no longer felt sick. The action of the heart was somewhat more regular. The appetite was better.
>
> "February 5. The patient had obtained some sleep. The sensation of fear that was always with him was gone. The respiratory frequency in the morning was 23. The cough was without difficulty.
>
> "February 6. The patient slept soundly most of the night, in a reclining position. The respiratory frequency in the morning: 20. The action of the heart was regular.
>
> "The heroin was then withdrawn for eight days. The ailments he had suffered before gradually returned. Heroin was again administered and had the same beneficial action as before."

Manges[9] who had previously reported on the advantages of heroin over morphine in the treatment of coughs, phthisis and asthma, reiterated his confidence in the drug in 1900.[10] Reviewing the treatment of the 341 respiratory cases by his colleagues, he stated that addiction was noted in less than eight per cent, without the bad effects accompanying morphine treatment. Where most of the cases included in Manges report did not show habituation, in two cases it had also been found to be successful in breaking addiction to morphine.

Prompted by Harnack's[11] warning in 1899, that heroin might be a dangerous poison, Turnauer[12] tested the drug for the possibility of harmful after effects. After treating 48 cases of phthisis, bronchitis and dyspnea, Turnauer noted a tolerance to the drug. After administering heroin for a long period, he found that the dosage needed to be increased. He stated that he found "No harmful results, especially as I observed no abstinence symptoms whatever. Generally it appeared that in all cases in which period of time was allowed to elapse the full effect could again be obtained with small doses ... It may be concluded that, regarding tolerance to heroin, certain individuals react peculiarly and it is recommended that in the case of old and feeble persons, the initial dose should not be over 0.005 g."

Horatio C. Wood[13] Jr., 1899, also found that the dosage had to be increased in order to remain effective. He warned, that experimentation was still not adequate to warrant the conclusion that heroin was not addiction producing.

Many other investigators recommended the use of heroin at the turn of the century. Most of them failed to refer to the danger in its usage or implicitly stated that it did not lead to tolerance.

In 1901, Joseph Jacobi, basing himself on the use of heroin in 85 cases, claimed the drug as superior as a cough-soothing remedy. Although he found its use more effective with patients who had never used strong narcotic drugs, he reported that any tendency towards tolerance could be averted if dosage was curtailed for several weeks. He also recommended that its use should be alternated with morphine or codeine.

At about this time the enthusiasm for heroin started to wane. Morel-Lavallée[15] in 1902 warned against its habit-forming properties although he thought it safer to use than morphine. Along with many others Morel-Lavallée advocated treatment by heroin in demorphinisation. His practice was criticized by Jarrige[16] in 1902 who claimed that physicians would thus make "heroinists" of their patients. Citing several cases of heroinism, he was emphatic in his contention that the withdrawal of heroin was much more painful than that of morphine. Rather than reducing the use of narcotics, the advocation of heroin was responsible for many persons becoming drug addicts.

In 1903 Pettey[17] reported that of the last 150 cases he had treated for drug addiction, eight were heroin users and of these, three had first become addicts through the use of heroin. He further reported that the heroin habit was just as difficult to cure as the morphine habit.

Sollier,[18] in 1905, deplored the use of heroin in the treatment of morphinism. This practice, he claimed, had resulted in the number of heroin addicts becoming as great as that of morphine addicts. Heroin was extremely toxic and the extent of poisoning in the heroinists he had seen, was much greater than it would have been for the same amount of morphine. Sollier found that the mental and physical deterioration from the use of heroin was very rapid. He opposed its use in the treatment of both morphinism and respiratory diseases.

In the same year Atwood[19] reported a case of heroinism in a woman who had become addicted to heroin after its use in surgery. Although not as vehement as Sollier and Jarrige, Atwood advised caution in prescribing the drug. Atwood believed cases of heroin addiction to be rare, but he pointed out that such cases would become more common if no discretion was used by the medical profession and he was against its prescription for coughs, recurring headaches, rheumatism and other chronic diseases.

At that time, however, there was no other drug that could fully replace heroin for some medical indications, and the medical profession was still in favour of it in spite of knowing many of its disadvantages.

As J. D. Trawick[20] of Kentucky expressed it (1911): "I feel that bringing charges against heroin is almost like questioning the fidelity of a good friend. I have used it with good results, and I have gotten some bad results, such as a peculiar bandlike feeling around the head, dizziness, etc., but in some cases referred to, it has been almost uniformly satisfactory."

Abuse of Heroin

It took a long time for the medical profession to realize the full danger of heroin addiction. On the other hand, very little time passed after the drug had become readily available before the underworld and smugglers discovered that heroin possessed properties even beyond those of other narcotics, which have since made it the main drug of addiction in many parts of the world. The analgesic and euphoric properties of heroin are much greater per gram than those of morphine.[21] There is no depression of the alimentary tract as is found in morphine. Whereas morphine usually is administered by a hypodermic needle, heroin can be sniffed into the system.[22] This is an important fact since many people are, to start with, repelled by the use of a hypodermic needle. However, persons addicted to heroin soon come to use it hypodermically and even intravenously. As the sensible effect wanes with increasing addiction, they try larger doses and more drastic methods of self-administration, always trying to recapture the stimulation of the drug. The addiction-forming properties of heroin are more pronounced even than those of morphine. It produces a disregard for the conventions and morals of civilization and these symptoms progress more rapidly than with other habit-forming drugs. Heroin addiction is the most difficult to cure; sudden withdrawal may lead to cramps, convulsions, and even to death from respiratory failure. The post-convalescent treatment, both psychological and physical, is longer and more difficult than with morphine.

Drug addiction is an international problem. The addicts preference however seems to vary greatly in different regions. In the Far East opium has been used as a narcotic for centuries,[23] in the middle East hashish.[24] In South America the chewing of coca leaves is an old habit.[25] Of the so-called "white drugs," the European addict has usually confined himself to cocaine and morphine.[26] There are three places in the world where heroin addiction has attracted more attention than any other drug addiction: U.S.A., especially the eastern part, Egypt, and China. In other places heroin addiction has been more sporadic.

The first place where heroin addiction seems to have been a major problem was the United States of America. The main site of the addiction was New York where 98 per cent of all drug addicts were reported at the time to be heroin addicts.[27]

The Public Health Service Hospitals in the United States discontinued dispensing heroin at its relief stations in 1916. In 1920 the House of Delegates of the American Medical Association at its 71st annual session adopted the following resolution: "that heroin be eliminated from all medicinal preparations and that it should not be administered, prescribed, nor dispensed; and that the importation, manufacture, and sale of heroin should be prohibited in the United States."[28]

Several other authorities, especially the police, supported this resolution. The growing number of crimes in the larger cities in the United States alarmed the public. In 1922 while there were seventeen murders committed in London there were 260 in New York City and heroin addiction was blamed for a number of the New York murders.[29] Carleton Simon, Special Deputy Police Commissioner in New York wrote (February 1924):[30] "Ninety-four per cent of the criminal drug addicts arrested in New York City use heroin regularly. Placing the consumers receiving their drugs from the illicit narcotic street venders in New York City at a minimum of 10,000 (based upon statistics of arrests), using at an average of ten grains a day per individual, we have a total of 76,000 ounces as the yearly quantity of heroin used by the narcotic addicts who procure their drugs on the streets in New York City alone." The entire amount of heroin prescribed by the entire medical profession in the State of New York was in the same period estimated to be fifty-eight ounces.

The result of these observations was a congressional law that prohibited the import of crude opium for the purpose of manufacturing heroin (June 1924).[31]

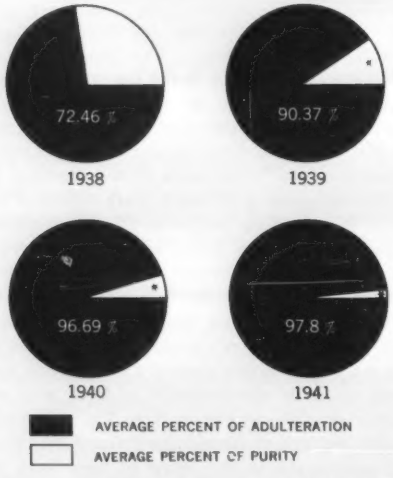
The production of heroin by pharmaceutical factories ceased within a very short time. As a substitute for

heroin, the factories concentrated their efforts on the production of codeine. The quantity of codeine substituted for heroin must be about two to six times the weight of the quantity of heroin originally used if a similar medicinal effect is to be obtained. Since there is little difference between the quantities of heroin and codeine produceable from a given quantity of opium, the quantity of opium required to be imported into the United States had to be greater after the enactment of the law. This is the main reason for the high opium import of the United States shortly after 1924.[32]

Although the legitimate production of heroin practically ceased after 1924, the addicts' demand for the drug continued to be supplied by smugglers. The heroin traffic in United States reached its peak in the last part of the 1920's. By 1930–1932, there was a sharp drop in the traffic due mainly to international restrictions. The heroin still in the illicit traffic was generally adulterated.

When World War II started, stricter border controls and lack of shipping lessened the illicit supplies of heroin. To stretch the supplies the traffickers resorted to more and more adulteration and dilution of the drug. The heroin finally obtained by the addict often contained less than two per cent of heroin. Many addicts were involuntarily cured, some without even realizing it. Others broke off the habit at least temporarily.

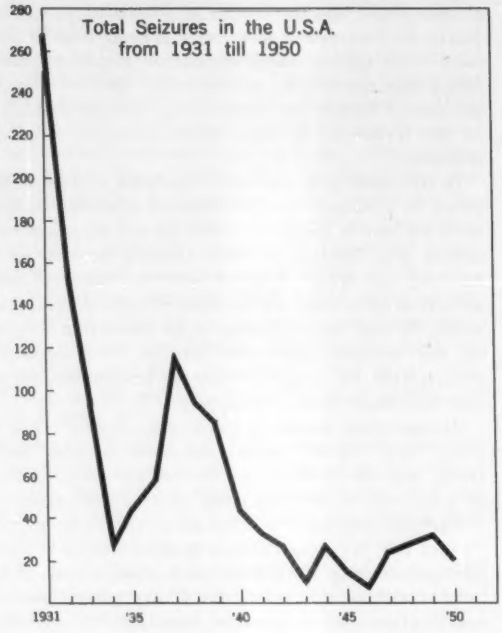
AVERAGE PERCENT OF ADULTERATION OF HEROIN FOUND IN ILLICIT TRAFFIC
CALENDAR YEARS 1938, 1939, 1940 and 1941



*By the time the drug reaches the addict, much of it is less than 1% pure.

As one stated: "If I could get good heroin or morphine again I would probably go back to using the drugs. As it is, I won't touch it as it has so much other stuff mixed with it that it is dangerous."[33]

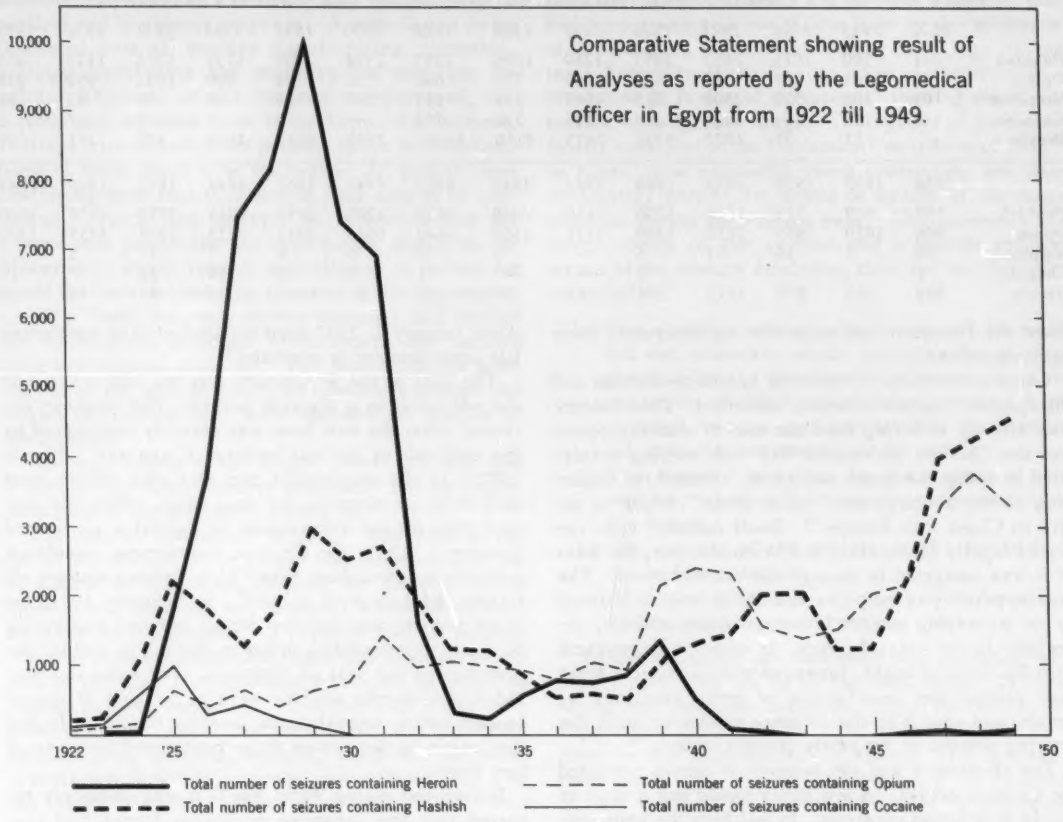
The following figures show the amount of seized heroin in the United States from 1930 till 1950:[34]



Another part of the world where heroin addiction attracted attention was Egypt. From ancient times hashish had been used as a narcotic in this country. The use of narcotics was however not such a serious problem before the "white drugs" came into the picture.[35]

This started in 1916, cocaine first being sold non-medically and shortly afterwards heroin. The price of the new narcotic was kept low to start with, until the vice had spread and caught large numbers of victims in its grip.[36]

There were even instances when contractors were paying their labourers with heroin.[37] The vice spread to every class of Egyptian society and a new kind of slum was formed as the result of heroin addiction. The hygienic conditions among the addicts were often beyond description and all sorts of sicknesses followed in the wake of heroin. Thus a great epidemic of malignant malaria started among the addicts in 1928, spread by the hypodermic syringe, which was injected into one person to the other without being disinfected after the use.[38] The total number of addicts in Egypt at the end of the 1920's has been estimated to half a million. Taking into consideration that the total population of Egypt at that time was about 14 million, the extent of the problem may be realized.



Before the first World War, there had been no drastic narcotic regulations in Egypt. The maximum penalty was 7 days' imprisonment or a fine of LE 1.[39] There had been no need for stronger measures. When it became evident that the heroin habit had become a serious problem, a new law was enacted which became effective in 1925. This new law made the trafficking in and the possession of narcotics illegal, classifying the offence as a "*délit*" with a maximum penalty of 1 year's imprisonment and LE 100 fine. During the first twelve months after the enactment of the new law, 5,600 prosecutions were made under it in Cairo alone. Within the year the maximum penalties were increased to 5 years' imprisonment and LE 1,000 fine. The new law made the drug traffic much more difficult in Egypt, but wholesale smuggling of the heroin began and increased in intensity until 1929. It is interesting to compare the number of seized heroin samples with the other narcotics in Egypt after the narcotic law in 1925. The number of seizures is a good indication of the traffic in narcotics. It seems from the table that the addiction to heroin in Egypt reached its peak in 1929 and from then on it dropped rapidly.

This drop after 1929 was due to two causes. The 1925 Convention on Narcotic Drugs had just come into effect and international measures quickly cut down the supply from all sources that made any pretense of legality. Also, new and vigorous legislation was enacted by the Turkish Government, and three big factories in Turkey were closed down. To start with, most of the illegal heroin in Egypt came from Europe,[41] but through stricter control these sources were closed and Turkey became the main source of supply. The manufacturers in Turkey transferred their equipment to other countries they thought to be more safe. Most of it went to Bulgaria where in a short time three or four larger factories were in operation.[42] One of the Bulgarian factories opened in October 1931 and in the first months turned out 1,500 kilogrammes of heroin which was smuggled out in trunks into Germany and France en route to Hamburg for the American market, and to Marseilles for the Egyptian and the Far Eastern markets. This new site of heroin production was discussed by the League of Nations Advisory Committee on traffic in opium and other dangerous drugs in 1931 with the result that the Bulgarian Government closed

TABLE SHOWING THE RESULTS OF ANALYSES AS REPORTED BY THE LEGOMEDICAL OFFICER IN EGYPT[40]

	1922	1923	1924	1925	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935
Hashish	241	500	1016	2465	1853	1260	1865	2935	2534	2789	1759	1214	1173	863
Opium	38	83	162	621	407	669	720	681	756	1433	989	1052	992	938
Morphine	105	105	590	2500	225	347	353	134	115	74	48	39	49	116
Cocaine	119	148	569	1000	226	426	220	122	—	10	5	5	7	1
Heroin	—	11	35	1872	3783	7475	8150	10000	7456	6947	1685	377	261	684

	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945	1946	1947	1948	1949
Hashish	569	609	574	1038	1296	1450	2048	2159	1269	1259	2211	3978	4238	4660
Opium	806	1020	955	2156	2388	2321	1569	1440	1644	2011	2235	3269	3753	3302
Morphine	25	7	14	21	3	—	5	2	6	8	7	17	5	7
Cocaine	1	—	—	—	9	—	—	1	2	8	16	12	7	13
Heroin	802	761	874	1375	594	113	18	1	—	—	29	38	13	30

down the factories and made the manufacturers once again homeless.

China now became a center of heroin production and the epidemic spread of heroin addiction. This country was already suffering from the use of smoking opium and the Chinese authorities had with varying results tried to stamp out opium addiction. Around the beginning of the century, the "white drugs" began to arrive in China from Europe.[43] Small amounts were imported legally for medical and scientific use, but most of it was smuggled in through the coastal ports. The greater potency of morphine and heroin was discovered by an increasing number of former opium addicts, especially in the coastal cities. In addition to products from the western world, Japanese pharmaceutical firms also started the manufacture of great quantities of heroin, and sent it to the Chinese market to fulfil the growing demand of the newly created addicts.[44]

The cheapness and the potency of heroin attracted the Chinese addict. A few cents would buy a dose of heroin or a heroin cigarette. In pill form the consumption of the drug is more secret and consumes less time than the opium smoking. Whenever the prohibition on smoking opium was periodically enforced by the Chinese Government, the consumption of the white drugs would increase since the absence of the opium odor and the opium pipe made it easier to evade the law. Even when opium smoking was tolerated on condition of registration, the white drugs retained their popularity, for the addicts feared to register because they would then be known and the government might at any time decide to cut off their supplies.[45] Because of civil war, revolutions, and war with Japan, the operation of the laws concerning narcotics in China have often been ineffective. The laws relating to the white drugs are the strictest that China has ever tried to enforce. The Provisional Regulations for the Drastic Prohibition of Highpowered Narcotic Drugs were promulgated in May 1934[46] to deal with the increasingly serious danger of manufactured drugs. According to these regulations, the penalty for the manufacture, transportation, and sale of highpowered narcotic drugs containing morphine, cocaine or heroin was death. The penalty for giving protection to those who manufacture, transport, or sell such drugs was also death. After January 1, 1937 even uncured addicts were given life imprisonment or executed.[47]

The goal of the government was the suppression of the addiction in a six-year period. The progress obtained under the new laws was abruptly interrupted by the outbreak of the war between China and Japan in 1937. In the unoccupied part of China efforts were still made to suppress the drug habit. When the six-year plan for the suppression of narcotics terminated January 1, 1941, the Chinese Government circulated a statement throughout Free China warning against all further indulgence of opium.[48] In February 1941, the death penalty was decreed for all persons cultivating poppies, manufacturing opium or narcotics, and for the distribution and sale of narcotics. The same law provided that heroin addicts were to be shot if apprehended taking injections or smoking heroin pills and that opium smokers were to be imprisoned from one to five years.

Before and during World War II it was commonly reported that the Japanese occupying forces had protected the manufacture and trade with heroin in their territories. This was confirmed after the war when large heroin factories were discovered by the Allies.[49]

The Commissioner of Narcotics of the United States reported that in one factory at Seoul, Korea, operated by the militarist Japanese Government of that time, 1,244 kilos of heroin were manufactured in 1938; and in 1939, 1,327 kilos. During these two years, while the Japanese occupied Manchuria, 2,400 kilos of this heroin were consigned to the Manchukuo Monopoly Bureau. The normal annual heroin requirements for China, including Manchuria, prior to 1938 were 15 kilos.

The total world medical needs for heroin for 1938 and 1939 were not more than 1,200 kilos for each year. Accordingly, the output of this one heroin factory alone was more than the total world medical needs for heroin.

INTERNATIONAL CONTROL OF HEROIN

The Hague Opium Convention of 1912 placed heroin in the same category as morphine and cocaine.[50] The Convention imposed an obligation on the Contracting Parties to "use their best endeavours" to limit the

manufacture, sale and use of the drugs exclusively to medical and legitimate purposes. A control was to be instituted over all persons manufacturing, importing, selling, distributing and exporting the drug and its salts. Registers of the amounts manufactured, imported, and exported were to be kept. Furthermore, dealings with unauthorized persons in the international trade of these drugs were forbidden. All preparations containing more than 0.1% heroin were also to be controlled. There was however no indication how the control over production and distribution should be implemented. Every country was allowed to decide for itself the best method. By the time of the outbreak of the first World War, only eleven countries had ratified the Convention, although seven others had notified their willingness to do so. The peace treaties after the end of the war, however, automatically brought the Hague Convention into force between the parties to the treaties.

The main defect of the Hague Convention was that it created no administrative machinery for the implementation of the principles agreed on.

The Geneva Convention of 1925[51] attempted to get rid of the defects of the Hague Convention and as far as heroin is concerned confined the manufacture to those establishments and premises alone which were licensed for the purpose. It required that all persons engaged in the manufacture, sale, distribution, or export of the drug should obtain a licence or permit to engage in these operations. It required also that such persons should enter into their books the quantities manufactured, imports, exports, sales and all other distribution of the drug. Under the system created by the Convention, the exporter is obliged to obtain from his government an export licence which will only be issued on production of the copy of an import certificate issued by the government of the importing country. A copy of the export authorization accompanies the consignment and must state the number and date of the import certificate so that it can be linked with it. Transit through a third country and the diversion of a consignment were also strictly controlled. By these means a strict check was made possible over the international trade in narcotic drugs. The Convention also abolished under the supervision of the Permanent Central Opium Board set up by the new International Instrument the exemption in the Hague Convention of 1912 for preparations containing not more than 0.10% of the drug.

The Geneva Convention came into force on 28 September, 1928.[52] The sharp drop in seizures of heroin both in United States of America and in Egypt shortly after the enforcement of the Convention began, clearly shows the considerable headway made in the control of the drug traffic. (See graphs on page 8 and on page 9.)

However, the controls brought about under this Convention did not limit directly the quantities of drugs to be manufactured. When in 1929 and 1930 the Egyptian Government reported the serious situation that had been created in the Middle East by the existence of uncontrolled factories in Turkey (see page 9), the tenth Assembly of the League adopted unanimously a resolution in favour of a system of limiting the manufacture of dangerous drugs. The system of limitation finally embodied in the Limitation Convention of 1931[53] is based upon estimates which contracting and non-contracting parties are asked to furnish of the drugs required during the coming year. The estimates are based solely on the medical and scientific requirements of the country furnishing them and are designed to include:

(a) The quantity necessary for use as such for medical and scientific needs, including the quantity required for the manufacture of preparations for the export of which export authorizations are not required, whether such preparations are intended for domestic consumption or for export.
(b) The quantity necessary for the purpose of conversion, whether for domestic consumption or for export.
(c) The amount of the reserve stocks which it is desired to maintain.
(d) The quantity required for the establishment and maintenance of any government stock.

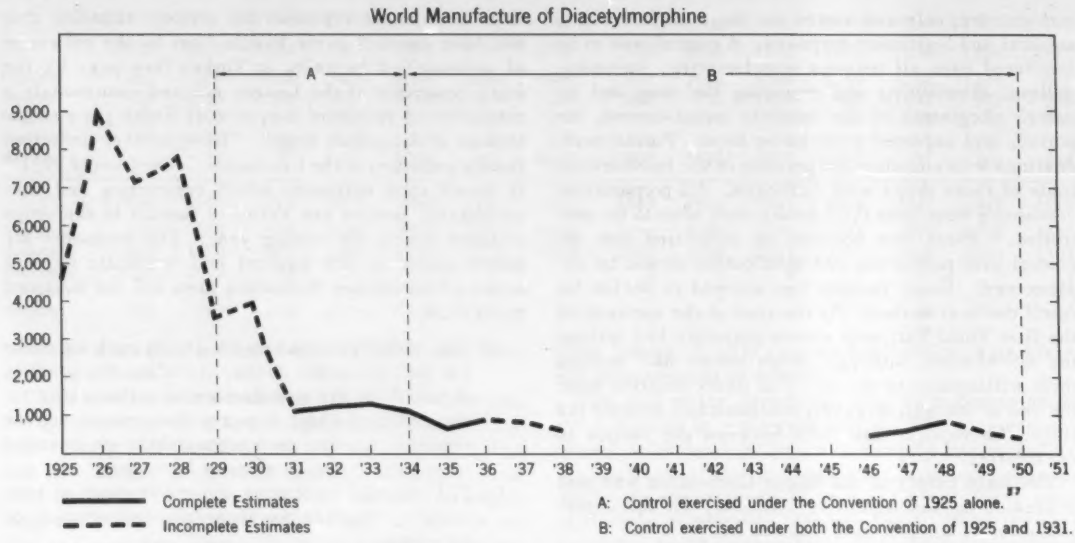
These estimates are examined and endorsed by a Supervisory Body set up by the Convention. In cases where the national estimates seem excessive, the Supervisory Body has the right to make recommendations to the governments concerned, with a view to their reduction. In case estimates are not furnished by any country, the Supervisory Body is empowered by Article 2 of the Convention to make the estimates itself. Special restrictions were laid on diacetylmorphine and its preparations by Article 10 of the Convention. Exports were prohibited, except on the request of the government of a country not manufacturing diacetylmorphine accompanied by an import certificate.

LICIT MANUFACTURE AND CONSUMPTION OF DIACETYLMORPHINE

The effect of the 1925 and 1931 Conventions will be seen from the production figures given below and the graph on page 12.[54] The figures show a drop in acknowledged heroin production from nearly 4,000 kgs. in 1930 to about 1,100 kgs. in 1934 and about 600 kgs. in 1935. The Permanent Central Opium Board reviews the progress of international control of drugs as follows:[55]

(November 1947)

"In the case of manufactured drugs, the period during which the international control can be described as having been world wide in scope is relatively short, the six years 1931-1936. This fact ... was due to events unrelated to the problem



itself, which resulted in a number of countries ceasing to furnish the Board with the statistics required. Nevertheless, the Board feels justified in stating even on the basis of the short period for which it has complete statistics, that some of the chief aims of the two conventions on the control of manufactured drugs—namely, a complete account of the supplies available (Geneva Convention of 1925) and the limitation of the manufacture to medical and scientific requirements (Limitation Convention of 1931) have been to a large extent and subject to one exception attained."

The exception mentioned concerned the illegal manufacture of heroin in Japan and Korea discussed previously. (See page 10.) It was estimated that from 1934 to 1937, 94 per cent of the world supply was accounted for. From August 1, 1946 the work of the Opium Section of the League of Nations was transferred to the Division of Narcotic Drugs of the United Nations.

As between pre-war and post-war there has been some changes in the proportion of the world's output produced by the heroin-manufacturing countries.[58]

	Average 1934–1937	*1948*
Japan	299 kgs.	—
USSR	162 "	—
Germany	60 "	—
United Kingdom	110 "	300 kgs.
Italy	90 "	276 "
Finland	— "	73 "
Other countries	184 "	184 "
	905 kgs.	835 kgs.

It is also interesting to note the pre- and post-war legal consumption of heroin in the various countries. (See graphs on pages 12–13.) Whereas in most countries, there has been a decrease in the consumption per million inhabitants, in a few others there has been a marked increase.

Present Stage of the Heroin Problem

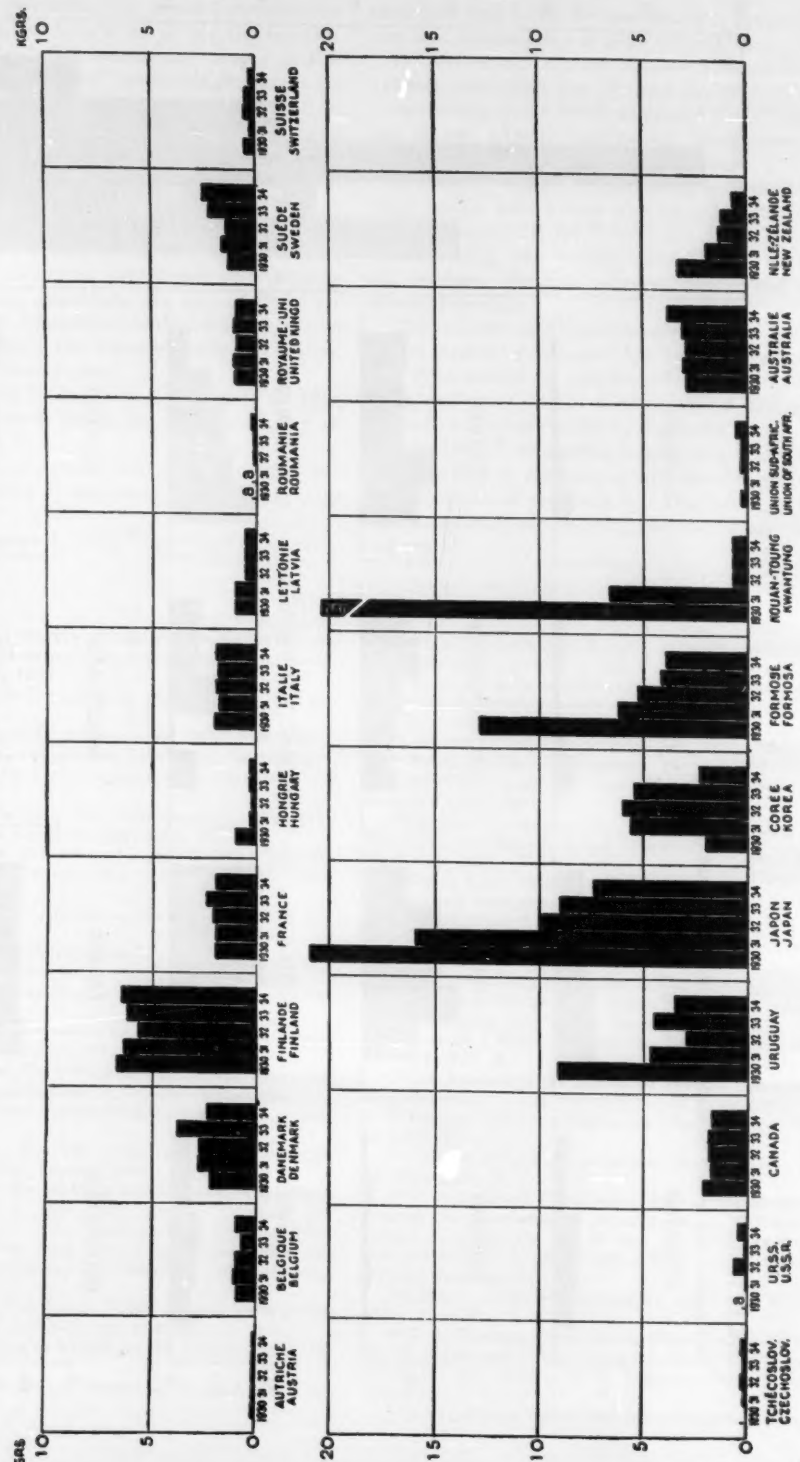
(The question of total suppression of heroin as a drug)

Due to the fact that in various parts of the world the heroin traffic has increased since World War II, creating conditions which have attracted the public's attention, such as the addiction among teen-agers in New York and other large cities in the United States,[58] the question of total suppression of heroin is being discussed by international organizations. The question of world-wide suppression of heroin production is not however of recent date. Such a proposal was made as early as 1923 in the Opium Advisory Committee which recommended the Council to request Governments to communicate their views as to the possibility of total suppression of the manufacture of heroin.[59] The replies from Governments indicated a division of opinion between the Governments which were willing to consider the possibility of total abolition and those which took the view that heroin is indispensable, for medical practice. The proposal for abolition was rejected by the Conference in 1925.[60]

At the 1931 Limitation Conference[61] a proposal was first moved for the total abolition of the use of heroin. This was objected to on the grounds that the drug was of medical value; that practically none was escaping into the illicit traffic for the amounts exported by manufacturing countries on the basis of import certificates, and that, even if heroin were abolished, it could be manufactured from morphine by any trafficker without any particular difficulty. In the result, the legal use

DIACETYLMORPHINE

Consumption per million inhabitants during the years 1930 to 1934.



DIACETYLMORPHINE
Consumption per million inhabitants during the years 1946 to 1950.
ARGENTINA
BELGIUM
DENMARK
FRANCE
FINLAND
38.15
HUNGARY
ITALY
UNITED KINGDOM
SWEDEN
URUGUAY
AUSTRALIA
UNION OF SOUTH AFRICA
NEW ZEALAND
NETHERLANDS
CANADA
SWITZERLAND
EQUADOR
1946 '47 '48 '49 '50

of heroin was not forbidden, but special restrictions were put on heroin, in Article 10 of the Convention. In reply to a circular letter sent by the League of Nations to governments in 1934[62] requesting opinions on the possibility of abolishing or restricting the use of diacetylmorphine, 12 countries communicated reasons why they did not feel able to consider abolishing or restricting the use of the drug. Four countries answered that they were in favour of restricting the use of diacetylmorphine, 8 countries stated that the use of the drug was already restricted *de jure* or *de facto* in their territories, 9 countries stated that they were in favour of completely abolishing the use of diacetylmorphine. Finally, 7 countries stated that the use of diacetylmorphine was in fact already prohibited in their territories by various measures.

The United States Government had already in 1924 prohibited the import of opium for the manufacture of heroin (see page 7).[34]

The Bulgarian Government had prohibited the importation, manufacture of and trade in heroin (25 July 1934).[63]

By decree of August 3, 1933,[64] the Spanish Government had prohibited the manufacture, import, distribution and consumption of diacetylmorphine.

In Costa-Rica[65] the use of diacetylmorphine had been entirely prohibited from October 24, 1928.

According to the Mexican Health Code[66] (from 1924) the import, export, preparation, possession, use and consumption of the drug was prohibited.

In Greece, heroin was excluded from the list of narcotic drugs whose use was permitted by the Greek State Monopoly (1930).[66]

From 1931, the Polish Government[66] prohibited in its territory the manufacture, import and export of diacetylmorphine.

The indispensability of heroin from the point of view of the medical profession has largely decreased since the introduction of dihydrocodeinone, dihydromorphinone and some of the new synthetic analgesics. In reply to a similar inquiry by the World Health Organization in 1950,[67] 38 member States have replied that they are in favour of dispensing with heroin, while 9 States are in favour of retaining it. The latter, however, includes several of the chief manufacturing countries of the world.

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The Use of Heroin in Therapeutics

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The campaign against drug addiction waged under the auspices of the United Nations raises two questions with particular reference to heroin:

Is the clinical use of heroin essential?

Is the addiction it produces so serious as to justify the drug's removal from the pharmacopoeia?

This is not the context for discussing why heroin is regarded as a specially dangerous narcotic drug, though it should be noted that observed cases of criminal offences due to its euphoric and mentally exciting effects seem to be rare in France.

Heroin is prescribed for therapeutic purposes essentially because of the pharmaceutical and dynamic properties that are peculiarly its own among the morphine derivatives and related synthetic substances, which are likewise habit-forming.

All pharmacologists agree that the physiological action of morphine is heightened by the acetylation of its two constituents, alcohol and phenol. Its analgesic effect is four to eight times as strong as that of morphine; its depressive effect on breathing is four times as powerful as that of morphine; since the respiration is deeper and stronger and since, as a result, the air cells of the lungs are effectively ventilated, the action of five milligrammes of heroin on the respiration is quantitatively almost equal to that of fifteen milligrammes of morphine; through its inhibiting influence on the central system, it has a well-recognized sedative effect on coughs.

These three properties in which heroin excels morphine and the other derivatives justify its clinical use in certain painful diseases characterized by coughing and difficulty in breathing.

Heroin is administered in pills, but most usually in solution, in liquid form or by subcutaneous injection. French practitioners do not employ intravenous injection. The daily dosage is from five to ten milligrammes (the maximum single dose), the maximum dose in twenty-four hours being twenty milligrammes.

Among the painful diseases only chronic complaints which have reached the terminal stage call for the use of heroin; it is not indicated for recurrent painful spasms. Such serious painful syndromes are essentially those of the painful types of cancer, especially those in which there is an invasion of the nervous system, or metastasis of the bone which have failed to respond to any other form of therapeutic treatment. Heroin, especially by injection, may be useful as a last resort after the action of other analgesics has been exhausted. Its potent analgesic and tonic action can greatly alleviate the sufferings of the final weeks of a patient afflicted with cancer.

Among the lung diseases the last stages of pulmonary tuberculosis may require the use of heroin. When anti-tuberculosis treatment has met with failure after failure—a contingency which will occur less and less frequently—and when the all too familiar picture of the consumptive who has reached the incurable stage of the disease becomes a reality, the physician should concentrate exclusively on relieving the patient. The advice which Professor Bard put into two words, "*opium et mentiri*," is an act of charity which the sufferer cannot be denied. During this final stage, heroin, by calming the distressing sensation of asphyxia, soothing the cough and leaving room for hope, can still be used as a valuable medicament which may succeed when all others have ceased to be effective.

Heroin should be used with greater caution, whether in solution or in liquid form, in the case of the curable or chronic types of pulmonary tuberculosis, where we personally advise against its use. It should be prescribed only in exceptional cases, such as infections of the larynx, in which the possibilities of antibiotics have been exhausted. In most cases, properly administered sedatives for the cough can yield equally satisfactory results.

Incurable mediastinal constrictions, whether caused by a cancerous growth, by a pathological condition of the mediastinal reticular lymph or by an aneurism of the aorta causing painful symptoms of asphyxia, may indicate that heroin should be used.

Appreciable use is once more being made of the opiates in the treatment of heart disease, owing to the influence of the work of Vaquez and his collaborators. In periods of asystole the opiates relieve anginal pains, insomnia, extreme distress and difficulty in breathing by their sedative action on the cortical and sympathetic nervous centres. The action of the muscles of the patient's heart is slowed by the resulting sleep and alleviation. Opium, by inducing calm and

relaxation, is the last hope of the patient dying of heart disease. Heroin may be used in such circumstances, on the condition, however, that it is only administered after light sedatives have proved ineffective, when the heart failure is acute and lasting, when the action of cardiac stimulants has failed and when it is decided to try something more potent than morphine and its derivatives.

These clinical uses are borne out by the figures for heroin consumption in the Paris hospitals. In the past few years it has been some 200 grammes annually (varying between 144 gr. and 308 gr.), with no regular decrease, whereas ten years ago the figure was approximately a kilogramme. It is remarkable how little heroin is now used; the 200 grammes consumed account for its use in the hospitals of a city of four million people. Half of the annual total is consumed by a large hospital centre for chronic and serious cases of tuberculosis and by anti-cancer centres.

The clinical use of heroin is only admissible on certain conditions:

(1) its use should not be merely routine or customary, but should be justified by the complete or partial ineffectiveness of other drugs;

(2) heroin should, as a rule, be used only for incurables who have not long to live and are in pain, irrespective of whether they are suffering from cancer, pulmonary tuberculosis or heart disease;

(3) the drug should be prescribed more cautiously in private practice than in hospitals, where the physician can control the dose and where it is practically impossible to encourage others to use the drug.

If these conditions are fulfilled, there are hardly any arguments in favour of the removal of heroin from the pharmacopoeia of countries which have clear and well observed legislation on the use of narcotic drugs. These are the conclusions reached by the Commission on Toxic Substances of the National Academy of Medicine in the report submitted by Professor Aubertin on 22 February 1949.

Without encroaching on a field which is not our own, we may express the thought that if morphine continues in current use, heroin is so easy to prepare that there is little point in banning it internationally. If there was any absolute need for prohibiting its use in therapeutics in order to combat addiction, the principle might conceivably be accepted; but if the effect of such prohibition were to be illusory, as we fear it would, it is hard to see why patients who may benefit from it need be deprived of it.

Furthermore, it is common knowledge that most heroin addicts are not recruited from the ranks of patients who have been cured, but from among morphine, cocaine or other addicts, whose addiction has very seldom been produced by the therapeutic use of a narcotic drug.

The rapid advances in modern therapeutics justify the belief that in many cases treatment by sedatives will diminish in scope. Surgical methods to relieve pain have already scored signal successes. Antibiotics now provide the best symptomatic treatment in cases of incurable tuberculosis, both for the cough and for the difficulty in breathing, the use of opiates declining gradually.

With these prospects in view, we feel that heroin should remain one of the therapeutic resources on which the medical profession can draw.

Heroin in the Official Pharmacopoeia

Since heroin began to be used as a medicine about the year 1900, official recognition of the drug has varied greatly. Several countries such as China, Mexico, Norway, Poland and Venezuela have never included any of the heroin preparations in their pharmacopoeias while other countries have officially recognized them and still do, and some countries have included them in some of their issues but later dropped them.

There are by now 12 countries which do not include heroin or heroin preparations in their official pharmacopoeias; these countries are: China, Denmark, Hungary, Japan, Mexico, Norway, Poland, Spain, Sweden, Venezuela, United States of America, and Yugoslavia.

The first country to make heroin an official drug was Austria. 1906. (Pharmacopoeia austriaca Ed. VIII).

The same year heroin and heroin hydrochloride were accepted, tentatively, by the Council of Pharmacy and Chemistry of the American Medical Association for listing in the proposed annual "New and Non-Official Remedies." The therapeutic indications of the compounds were given as follows: "When given in small doses heroin hydrochloride has apparently no effect on any of the vital functions except respiration ... In large doses it may produce dizziness, nausea and occasionally constipation and in poisonous amounts, twitching of the extremities, great exhaustion and dimness of vision ... The habit is readily formed and leads to the most deplorable results... On withdrawing the drug from habitues, there is said to be a tendency to respiration failure ... Heroin and its hydrochloride are recommended chiefly for the treatment of diseases in the air passages attended with cough, difficult breathing and spasm, much as the different forms of bronchitis, pneumonia, consumption, asthma, whooping cough, laryngitis and certain forms of hay fever. It has also been recommended as an analgesic, in the place of morphine in various painful affections."

In the United States, official acceptance of the drug came in 1910, with the inclusion of diacetylmorphine and its hydrochloride in the United States Pharmacopoeia IX. The drugs were, however, withdrawn from the next edition, U.S.P.X. published in 1920. Eighteen countries still include heroin and heroin preparations in their pharmacopoeias: Argentina (Farmacopea Nacional Argentina, Ed. III, 1943), Austria (Pharmacopoea Austriaca, Ed. VIII, 1906), Belgium (Pharmacopée belge, Ed. IV, 1930), Brazil (Pharmacopeia dos Estados Unidos do Brazil, Ed. I, 1929), Finland (Pharmacopoea Fennica, Ed. VI, 1937), France (Codex Medicamentarius Gallicus, Ed. VII, 1949), Germany (Deutsches Arzneibuch, Ed. VI, 1926), Greece (Hellenike Pharmakopoiia, Ed. II, 1924), Italy (Farmacopea Ufficiale de Regno d'Italia, Ed. VI, 1940), The Netherlands (Codex Medicamentorium Nederlandicus, Ed. V, 1926), Paraguay (Proyecto de Farmacopea Paraguaya, 1929), Portugal (Farmacopeia Portuguêsa, Ed. IV, 1946), Romania (Farmacopea Română, Ed. IV, 1926), Switzerland (Pharmacopoea Helvetica, Ed. V; 1949), Turkey (Turk Kodeksi, 1940), Union of Soviet Socialist Republics (Gosudarstvennaia Farmakopeia Soiuza Sovetskikh Sotsialisticheskikh Respublik, Ed. IX, 1952), United Kingdom (The British Pharmacopoeia, 1948).

The Austrian, Dutch and Finnish pharmacopoeia include both Heroin and Heroin hydrochloride, while the rest list just Heroin hydrochloride.

The Greek Pharmacopoeia of 1924 is no longer up to date in regard to narcotics. Heroin has not been used in Greece since 1930, because of its exclusion from the list of narcotic drugs whose use is permitted by the Greek State Monopoly.

The following preparations are listed in the "British Pharmaceutical Codex 1949":*

Elixir Diamorphinae et Terpini

Composition:

Diamorphine hydrochloride	0.91 g
Terpin Hydrate	4.6 g
Alcohol (90 per cent)	250 ml
Glycerin	250 ml
Syrup of Wild Cherry to	1000 ml

Elixir Diamorphinae et Pini Compositum

Composition:

Diamorphine Hydrochloride	0.46 g
Terpin Hydrate	4.57 g
Oil of Pumilio Pine	8,3 ml
Alcohol (90 per cent)	250,0 ml
Glycerin	250,0 ml
Compound Solution of Tartrazine	10,4 ml
Sucrose	400,0 g
Water to	1000.0 ml

Linctus Diamorphinae

Composition:

Diamorphine Hydrochloride	0.91 g
Oxymel	333,3 ml
Glycerin	333,3 ml
Compound Solution of Tartrazine	12,5 ml
Syrup to	1000,0 ml

Linctus Diamorphinae et Hyoscyami

Composition:

Diamorphine Hydrochloride	0.91 g
Tincture of Hyoscyamus	75,0 ml

Linctus Diamorphinae et Hyoscyami *(Continued)*

Composition: *(Continued)*

Emulsion of Chloroform	75,0 ml
Syrup of Tolu	150,0 ml
Syrup of Wild Cherry	150,0 ml
Glycerin to	1000,0 ml

*A new British Pharmacopoeia (1953) has been issued since the preparation of this paper. It has not yet been possible for the Editors to consult this issue. Neither has it been possible to consult the official pharmacopoeias of Czechoslovakia and Chile.

The United States Bars the Manufacture of Heroin

On April 3rd 1924, the Committee on Ways and Means of the House of Representatives* met for a hearing introduced by the Hon. Stephen G. Porter, a Representative in Congress from the State of Pennsylvania, proposing to amend the Acts of 14 January 1914, and 26 May 1922 entitled "The narcotic drugs import and export Act" by the addition of the following sentence:

> "*Provided*, that no crude opium may be imported for the purpose of manufacturing heroin."

It might be of interest to the readers of this special issue of the "Bulletin" to have an account of this hearing, since it gives the main reasons which led Congress to accept the amendment proposed by Mr. Porter.

Before introducing his bill, Mr. Porter sent a series of letters to prominent physicians, judges, city magistrates and police and prison authorities in order to ascertain their views. He did not overlook, as Chairman of the Foreign Affairs Committee of the House of Representatives, the international implications of his proposal.

For many years Mr. Porter had studied the problem of narcotic drugs and drug addiction and in introducing his amendment he explained that he had come to the conviction that heroin was the most dangerous of all the habit-forming drugs, that it was responsible for a large amount of crime, although the medical profession, with a few exceptions, looked upon it as a comparatively useless drug. He pointed out that the Army, the Navy, the Public Health Service, the Veteran's Bureau and the American Medical Association had all condemned its use on the ground that it is entirely too dangerous and had no medical value that cannot be supplied by codein or other drugs.

In support of his assertions Mr. Porter introduced extensive written testimony. Moreover, the Committee on Ways and Means heard statements by:

Dr. Rupert Blue, United States Public Health Service,

Sidney W. Brewster, Assistant superintendent and deputy Warden, Reformatory Prison, Hart's Island, New York City,

Dr. Charles W. Richardson, Washington, D. C., and,

Dr. Amos O. Squires, Chief physician, Sing Sing Prison, Ossining, N. Y.

The main reasons given in support of the condemnation of the use of heroin might be summarized as follows:

(1) *The medical usefulness of heroin is negligible compared with its evil effects; the drug can easily be replaced by one of the other alkaloids of opium with the same therapeutic effects.*

In an order dated 2 December 1916, circular letter No. 102 by the Public Health Service, the Surgeon General pointed out that "heroin as a palliative in certain respiratory affections serves no purpose which cannot be accomplished by other agents fully as effectively and without the attendant possibility of great disaster."

On 25 March 1918, the Secretary of the Treasury, Mr. McAdoo appointed a committee to investigate the traffic in narcotic drugs. The report of this committee, submitted in June 1919, concluded with the following statement:

> "It is the opinion of the committee, based on the results of its investigations, that the medical need for heroin, a derivative of morphine, is negligible compared with the evil effects of the use of this alkaloid, and that it can easily be replaced by one of the other alkaloids of opium with the same therapeutic results, and with less danger of creating habituation."

In 1920 the Surgeon General of the Public Health Service forwarded a questionnaire on heroin to some of the leading physicians and surgeons of the United States. Sixty-six physicians replied to the question as to whether heroin could be replaced in medical science by the substitution of codein or morphine. Of this number 46 voted in the affirmative and 20 in the negative.

Mr. Hawley: "You think that is a fair average of how the medical profession generally would vote, or would there be a stronger opinion in favor of the suppression?"

Dr. Blue: "I think if the facts which have been brought before your committee to-day were generally

*When a bill is introduced in either branch of Congress of the United States, the usual practice is to refer the bill to the appropriate Committee of the Senate or of the House of Representatives for consideration. This Committee holds hearings which for the most part are open to the public and at which any persons interested may appear and present arguments either in favour of or against the proposed legislation.

known, the profession would be pretty nearly unanimously disposed towards its suppression."

Mr. Hawley: "You think they would follow the conclusions of the American Medical Association?"

Dr. Blue: "Yes, Sir."

Dr. Richardson, when giving his testimony before the Committee of the House of Representatives, made reference to a resolution adopted by the House of Delegates of the American Medical Association at its New Orleans' meeting in 1920. Dr. Richardson explained that the House of Delegates was the law-creating body of the American Medical Association which represented at this time 90,000 physicians in the United States. The resolution read "That heroin be eliminated from all medical preparations. And that it should not be administered, prescribed, nor dispensed, and that the importation, manufacture, and sale of heroin should be prohibited in the United States."

Dr. Richardson stated further, answering a question upon what effect heroin produces that can not be obtained by cocaine or morphine, and whether he could name a case where heroin would be used to very great advantage over other derivatives from narcotic drugs, that "Heroin when first introduced was supposed to be an unusually valuable drug in certain conditions, especially where morphine as a sedative was required. For instance, in my work in medicine it was largely used to allay cough—it is very valuable in that work —and in this administration many of us have observed that our patients demanded more of the drug. They were forming the habit, and I want to tell you, that in nearly eight years, I have not written a prescription for heroin." And then, replying to a question as to whether he had found other drugs that would take the place of heroin, he said, "Absolutely. Sometimes they produce headache and nausea, but they have the physiological effect. The only thing about heroin is that it is more pleasant to take." Dr. Richardson explained moreover that, if morphine produced sickness and nausea, there was another derivative of opium, namely codeine, that was "nearly as good as morphia," which could replace heroin.

Dr. Rubert Blue pointed out that the action of the United States Public Health Service was based on the belief that the administration of the drug was dangerous and that the need for a respiratory sedative in medicine could be met by using codeine, where there is less danger of creating habituation.

(2) *Heroin is a dangerous narcotic drug with pronounced physiological and psychological ill-effects.*

Dr. Blue, testifying before the Committee, explained that heroin resembles morphine in its general effects, but acts more strongly on the respiration, and is, therefore, more poisonous. While heroin does not cause constipation, it does undoubtedly create habituation even to a greater degree than any other drug.

It is used chiefly to allay cough in certain diseases. Some authorities claim that in addition to its general effect heroin inflates the personality and exaggerates the ego to a dangerous extent.

He made reference to the opinion of the American Medical Association, as formulated by a committee appointed by that Association to study the narcotic drug situation in 1920.

He then quoted the opinion of a series of physicians:

Dr. Bastedo, of the Medical Department of Columbia University, concludes, after an exhaustive investigation and prolonged study of these drugs, that heroin is not an effective or safe substitute for morphine or codeine.

In a number of tests codeine proved superior in its power to allay cough, to overcome pain, and to promote sleep. Like morphine, heroin is the cause of a vicious habit.

Professor Cushney, of Edinburgh, states that the advantages claimed for heroin (action on respiration) by its advocates, have not been confirmed by an impartial investigation.

The Viennese expert, Professor Knaffl-Lenz says that:

> "Heroin is incomparably more poisonous than morphine, and the therapeutic dose is not appreciably smaller than the toxic dose. For this reason, German pharmacologists warned physicians from the beginning against the use of this remedy, and pronounced it to be not indispensable."

It therefore does not satisfy the requirements of a substitute for morphine. He goes on to state that it is much more suitable for abuse than morphine, and produces physical collapse more rapidly than that drug. In view of these facts, heroin has never been used to any great extent in Germany or Austria, and hardly at all in nursing homes and public hospitals in those countries.

Answering the question as to whether the use of heroin shortens life of an addict, that is, as to whether the addict of heroin dies quicker than the addict of morphine, Dr. Blue stated that "the drug being more poisonous," he thought it does shorten the life of an addict more rapidly than would morphine.

The following exchange of views then took place between a Committee member and Dr. Blue:

Mr. Hawley: "Why is it a more dangerous habit-forming drug? What is the physiological reason for that?"

Dr. Blue: "I might enumerate the causes of addiction in reply to that question. In considering that phase of the problem, I would place the excessive production of narcotic drugs, the association with addicts, and persuasion by drug peddlers, as the chief causes."

Mr. Hawley: "Are those the causes that lead to its use?"

Dr. Blue: "Yes. The small dose and bulk facilitate smuggling and secret addiction."

Mr. Hawley: "Why is it the most dangerous habit-forming drug? What is the reason for that?"

Dr. Blue: "It produces physical and mental collapse more rapidly than any other habit-forming drug."

Mr. Hawley: "Does it create an appetite for itself?"

Dr. Blue: "Yes, authorities say that a dangerous drug is one which produces a marked tolerance leading to an increase in dosage, craving for the effects of the drug, and disregard of the disagreeable after-effects. Heroin possesses all of these properties."

It was further explained to the Committee that there was another reason for the popularity of heroin among addicts, i.e., the facility with which it could be taken.

One of the members of the Committee asked a witness whether addicts always snuffed heroin. The following discussion then took place:

Dr. Squires: "No; but it is one of the very frequent ways of using it, by snuffing it. And among the criminals it is no uncommon thing, if they cannot get a hypodermic needle, to take an ordinary pin and poke a hole in their arm and take the heroin and rub it over the hole. We find that very common."

Mr. Dickinson: "Is it ever taken by capsule in the mouth?"

Dr. Squires: "Yes; you can take it internally, hypodermically, or snuff it. It is a very convenient drug to take."

Mr. Dickinson: "But you can take it by capsule in the mouth just like morphia?"

Dr. Squires: "Yes, or in tablet form. You can buy the heroin powder and put it in a capsule, or you can have the heroin tablet made."

Mr. Dickinson: "And swallow it?"

Dr. Squires: "Yes."

Mr. Treadway: "In what form is it generally peddled?"

Dr. Squires: "In powder. They sell it in powder. They have what they call 'decks,' heroin put up in so many little powder papers."

Dr. Squires explained also to the Committee that the addict began generally with a small dose and then increased it gradually in order to get the same results. He said that some of the addicts took more than they really ought to take, or should take, because they were afraid they would not get enough. According to Dr. Squires, the amount that they took was "really tremendous." He cited cases when the addict took as much as 80 grains a day, the average for an addict being 15 to 20 grains. To the question what was the toxic dose, Dr. Squires answered that this depended on the individual make-up, adding "The medicinal dose is one-twentieth to a sixth of grain. I would hesitate to take a grain, although I might take it and get away with it."

(3) *There is a link between heroin addiction and crime.*

Early in the Committee's proceedings Mr. Porter made reference to a memorandum in which Dr. Alexander Lambert, of New York, stated that "Heroin cuts off the sense of responsibility in the moral sense much quicker than morphine. It destroys the sense of responsibility to the herd. Heroin addicts will more quickly commit crime and with no sense of regret or responsibility for it. The herd instinct is obliterated by heroin, and the herd instincts are the ones which control the moral sense in the sense of responsibility toward others and the environment in general. Heroin obliterates responsibility the same as cocaine, and it makes much quicker the muscular reaction, and therefore is used by criminals to inflate them, because they are not only more daring but their muscular reflexes are quicker."

Moreover, Mr. Porter reported to the Committee that he had written to Mr. William McAdoo, police magistrate of New York, asking for his authorization to quote the following statement:

> "We committed last year from this office about 900 drug addicts and I should say that 98 per cent are users of heroin. Very rarely do we run across a case where the addict is taking morphine or cocaine."

And further among one written testimony introduced by Mr. Porter, Dr. Herman N. Bundeson, Commissioner of Health of Chicago, said that "I think criminologists the world over will tell you that the violent crimes are the ones that are committed by heroin addicts."

Dr. Richardson stated during his testimony that "This question of heroin habituation and its production yearly of enormous numbers of new criminals is one of the most important moral questions that is up before the American Government at the present time" and later, speaking about the effects of heroin on addicts, he said: "That is one of the things it does, dethrone their responsibility. It gives them an exalted impression of their own importance, and criminals by using it obtain this result." Dr. Richardson concurred with the observation made by a member of the Committee, that under these circumstances "no business transaction of any kind would be really dependable with heroin addicts."

Dr. Squires explained that at the Sing Sing Prison, prior to 1919, the question of drug addiction was not of the same great concern, as it had been during the last years. In 1917, out of the total number received at the prison, less than four-tenths of one per cent were drug addicts. Prior to 1919, for an average of six years, drug addicts would only equal about 13 a year. In 1920 it increased over 100 per cent over that average. In 1922 it increased over 500 per cent over that average, and in 1923 it increased over 900 per cent. "So to-day, said Dr. Squires, one out of every eleven men who is admitted to Sing Sing prison is a drug addict. They are what you might call criminal drug addicts."

Additional figures were brought before the Committee by Mr. Brewster who said that approximately 60 per cent of the inmates at the reformatory prison at Hart's Island, and 100 per cent of the inmates at Riker's Island, where they go first for the cure, were drug ad-

dicts; and about the same proportion at the penitentiary at Hart's Island. At the Woman's Workhouse, Black Wells Island, practically all prostitutes committed were drug addicts. Sixty to 80 per cent of all committed there were drug addicts. Of these drug addicts, from 90 to 95 per cent used heroin.

Data were also submitted to the Committee concerning the Leavenworth and the Atlanta penitentiaries showing the rapid increase in the percentage of prisoners who were drug addicts.

The figures for the Leavenworth penitentiary are as follows:

	Average population	*Prisoners received*	*Violation drug act*	*Drug addicts*
1914	1,019	463	15	3
1915	1,160	936	15	12
1916	1,664	1,116	48	47
1917	1,677	705	31	29
1918	1,613	1,144	53	50
1919	1,895	1,300	57	72
1920	1,800	1,147	94	64
1921	1,721	1,205	247	64
1922	2,242	1,686	498	263
1923	2,473	1,482	717	299

From 1 July 1923 to 31 October 1923, 417 prisoners were received. Of this number 138 were for violation of the Harrison Narcotic Act and 41 admitted they were habitual users of narcotics.

For the Atlanta penitentiary the figures were as follows:

	Number of prisoners or inmates in institution for the year	*Number of addicts in same year*	*Per cent*
1914	453	—	—
1917	812	—	—
1918	1,216	134	11
1919	1,171	71	6
1920	1,492	128	8
1921	1,508	235	15
1922	1,707	352	20
1923	1,847	336	18

It was pointed out, however, and this was confirmed by other statistics submitted to the Committee that the figures concerning the Leavenworth and Atlanta penitentiaries were higher than those relating to State prisons since the prosecutions of the violations of the Harrison Narcotic Act were tried in the United States courts and the prisoners sent to the above mentioned penitentiaries.

During Dr. Squires' testimony the following discussion took place between him and Mr. Porter:

Mr. Porter: "Pardon an interruption, but the reason they commit the crime is their frenzy to get money with which to buy more drugs, is it not?"

Dr. Squires: "A large percentage of them, yes."

Mr. Porter: "It is not a desire to commit a crime, but the desire to get money with which to buy drugs?"

Dr. Squires: "A large percentage of our men are there for grand larceny, because the taking of the drug is a very expensive luxury."

Mr. Porter: "Do you recall that case in your State where four or five addicts went into a bank and shot the cashier and clerk?"

Dr. Squires: "Yes, of course that is a rather common crime."

Mr. Porter: "They were all addicts?"

Dr. Squires: "Yes, and the drug addict, they tell me, will spend as much as $48 a day to secure these drugs from the drug peddler. The drug is adulterated with sugar or milk, and they have to buy a lot in order to satisfy their craving."

The Chairman: "As I understand it, then, Doctor, they commit crimes in order to get money to buy this drug?"

Dr. Squires: "Not all of them; no, some of them do."

The Chairman: "In some instances they do?"

Dr. Squires: "Yes."

The Chairman: "Now, right in that connexion, I would like to ask another question. Do they commit crimes while they are under the influence of the drug —that is, does the drug create such a state of mind that they are more reckless?"

Dr. Squires: "Yes, some of them never would commit the crime if they were not in the state of intoxication due to the drug. Others will take it when they are more themselves, but the craving is there and they will commit the crime in order to get the money in order to satisfy their craving."

Mr. Porter: "Doctor, can you tell the Committee the percentage of the gunmen in New York who commit crimes of violence, who are addicted to the use of drugs?"

Dr. Squires: "I could not tell you that."

Mr. Porter: "Well, a great many of them are?"

Dr. Squires: "A great many of them are. A man who takes heroin is particularly reckless."

A similar opinion was expressed by Mr. Brewster in the course of his testimony:

Mr. Porter: "Now, from your experience as a criminologist, do you believe that many of the crimes of violence committed in and about New York City are due to addicts who are unable to secure the drugs, and in their frenzy commit these crimes for the purpose of securing money with which to buy drugs?"

Mr. Brewster: "In my opinion, I think there are a large number."

Mr. Porter: "Am I correct in this conclusion? That the purpose of the confirmed criminal in taking heroin before perpetrating a crime of violence is to relieve himself of moral restraint?"

Mr. Brewster: "That is my opinion; and that is also true of cocaine. I would say this, that users of morphine, while they do commit crimes, they are not usually crimes against the person; they are not usually crimes of violence. They are such crimes as theft, forgery, or something along that line. The man who

uses heroin is a potential murderer, the same as the cocaine user; he loses all consciousness of moral responsibility, also fear of consequences."

And at another time during his testimony, Mr. Brewster said that in many cases the leaders of the various gangs of gunmen do not use narcotics themselves but when they send out members of the gangs on a crime to commit murder or robbery, they see that they are well "charged" before they go, usually with heroin.

During his testimony Dr. Squires, answering Committee members' questions, defined the state of mind of heroin addicts as follows:

Mr. McLaughlin: "Others who have testified have stated that at more length than you have that the use of heroin induces a criminal state of mind."

Dr. Squires: "It makes them reckless, and it inflates their personality. They are a good deal like a patient with paresis; the world is theirs, as it were. It inflates their personality to the extent that it makes them have a feeling of grandeur."

The Chairman: "And do they in a measure lose their sense of right or wrong?"

Dr. Squires: "They do, indeed. They do not regard the property or person of another. But, as I say, just as you can expect that the influence upon any individual depends upon that individual, the same thing holds true with any drug. There are some people who take heroin and would not commit a crime at all, and there are others that it makes it easy for them to become criminals."

Dr. Squires pointed out further that about 50 per cent of the addicts came back to prison. He confirmed a statement made on a previous occasion that he believed "that a large percentage of the men who are convicted of a crime, who are drug addicts, would not have committed the crime if they had not been influenced by the drug habit." He also confirmed a statement that "probably 75 per cent of the drug users admitted to prisons take heroin."

In the written testimony introduced before the Committee by Mr. Porter a letter of the Department of Health of the City of New York is of particular interest since it confirms the high percentage of heroin addicts among drug addicts and the fact that they acquired it through evil association. The letter is entitled "Should the manufacture of heroin be interdicted" and reads as follows: "It is our opinion that interdiction is indicated owing to the promiscuous and improper use of this drug by the addict and the rather infrequent use of this drug in general medical practice.

"The narcotic clinic operated to study first-hand drug addiction by the Department of Health of New York City demonstrated that of 7,464 narcotic drug addicts over 90 per cent of them were addicted to the use of heroin.

"In 69 per cent of the total clinic applicants the drug-habit had been acquired through evil associates. The vast proportion of these were all under 30 years of age.

"The recent report of special deputy police Commissioner of New York City regarding three years experience in scrutinizing the "dope" evil is also corroborating, at least statistically.

"Of 9,637 persons arrested in the three past years 6,892 were addicted to heroin or cocaine, singly or combined.

"The average age of the addicts in 1921 was 25 years, while in 1923 it ranged between 27 and 28 years.

"This official, also a physician, also reports that only two per cent of those arrested can trace their addiction to medical treatment. The major causes were found to be "curiosity, morbidity, and criminal association."

"Hence, we may conclude that 98 per cent of nearly 10,000 drug addicts acquired their vice through curiosity, morbidity, and criminal association and that 71 per cent of the total were users of heroin."

In another written testimony Dr. S. Dana Hubbard states: "...Heroin is the drug used by addicts of over 95 per cent of New York's underworld (criminal classes), according to the statistics of the police and prison statistics, and the unfortunate part of the situation is that less than 1 per cent of these miserable creatures acquire the habit through illnesses.

"...The heroin question is not a medical one, as heroin addicts spring from sin and crime. It is a social problem where the medical and pharmaceutical and allied professions can do much to aid in solving this serious problem.

"Society in general must protect itself from the influence of evil, and there is no greater peril than that of heroin."

In a memorandum quoted by Mr. Porter, Judge Cornelius F. Collins, Justice Court of special sessions, City of New York (December 1918) points out that: "At least one-tenth of the whole of the business of the Court of Special sessions of New York County is made up of drug addicts, those possessing the drug or having dealt in it in some way. This means 10 per cent of all cases coming into our Court, a large part of which do not involve moral turpitude. In addition to the number of these addicts, as such, come quite a large number charged with larceny, assault, unlawful entry, and the like, who are nevertheless addicts, so that it is safe to say that in 20 to 30 per cent of the cases coming into the Court of special sessions involving moral turpitude the culprits are given to drug addiction in some form or other."

(4) *Action taken by Federal or International Bodies and the Medical Profession against the use of heroin.*

During the Committee's discussions Dr. Richardson answering to an observation stating that it appeared that the movement against the use of heroin actually started in a Federal Department, the United States Public Health Service said: "Yes; primarily, but the medical profession was awakened to the necessity.

The Public Health Service started it, but the Public Health Service made more headway with it simply because they could control their men more directly than the medical men in general control their patients." It was then established that the action of the United States Public Health Service taken in December 1916 had been followed four years later by the resolution of the House of Delegates of the American Medical Association at its New Orleans' meeting in 1920 referred to above. The circular directing the discontinuance of the use of heroin was to the following effect:

> "In view of the fact that the great increase in the use of heroin at present constitutes a considerable menace to public health in the United States, it is desired to set an example and to signalize to the general public the danger which may accrue from its use. Heroin as a palliative in certain respiratory affections serves no purpose which can not be accomplished by other agents fully as effectively and without the attendant possibility of grave disaster.
>
> "You are therefore directed to discontinue dispensing heroin and its salts at relief stations of the service, and to send all the stock of these drugs now on hand to the purveying depot, 1414, Pennsylvania Avenue N.W., Washington, D. C., either by parcel post or by freight on Government bill of lading.
>
> "Rupert BLUE, Surgeon General."

Three years later, on 29 December 1923, General M. W. Ireland, Surgeon General of the United States Army, issued an order that heroin should cease to be given to members of the Medical Corps of the United States Army, and all offices and posts where heroin or its derivatives or preparations were held were ordered to return it to the depots.

On 2 February 1924, the Surgeon General of the United States Navy, Admiral Stilt issued an order stating that "further issues of heroin to the United States naval service have been prohibited."

Finally, on 10 March 1924, George E. Ijams, Assistant Director of the Medical and Rehabilitation Service of the United States Veterans' Bureau sent a circular stating that "This bureau does not approve of the administration of heroin to any of its beneficiaries. This decision is based on the best medical authority. Heroin shall not be issued in future to any member or unit of the Veterans' Bureau and such stocks as may be on hand shall be forwarded to the nearest supply depot."

Dr. Rupert Blue stated that the suppression of dangerous and unnecessary drugs is interesting the world, as reflected in the action of the International Office of Public Health at Paris. In April 1923, upon the suggestion of the American delegate to the Office, this representative body of medical men issued through the French Foreign Office a circular letter to the signatory powers requesting information relative to the advisability of suppressing heroin. Up to October 1923 replies received which indicated that the majority of the governments would vote in the affirmative. The Italian delegate presented the results of the inquiry made in Italy. Of 58 physicians to whom the questionnaire had been sent, 30 voted in favour of the suppression and 18 against.

The question of the suppression of heroin had also been considered by a committee composed of members of the Advisory Committee on traffic in Opium and other dangerous drugs, and the Health Committee of the League of Nations. In 1923 this Committee adopted the following resolution:

> "In view of the fact that a question is being raised as to the possibility of prohibiting the manufacture of heroin, the sub-committee thought it might give its opinion from the medical point of view and might state that the Mixed Sub-Committee, composed of technical experts, agrees, having regard to the small therapeutic value and harmful effects of diacetyl-morphine, to advocate the prohibition of its manufacture."

(5) *Barring the manufacture of heroin would strengthen the position of the United States in International Narcotic Conferences.*

It is of universal knowledge that the first step in the international campaign against narcotic drugs took place in 1909 when an International Opium Commission met in Shanghai on the initiative of the United States Government.

The fact, however, that for a certain time the domestic legislation in the field of narcotic drugs remained behind the generous intentions of the United States Government thwarted the action of this Government in international gatherings relating to narcotic drugs.

Thus, rendering account of the 1912 Opium Conference at The Hague, Mr. Hamilton Wright wrote:

> "There is no doubt that during the sittings of the International Opium Conference at The Hague, the American delegation was placed in a somewhat embarrassing position owing to the neglect of the Congress to pass legislation which had been urged upon it by the Executive, aimed to perfect the opium-exclusion act of February 1909, and to bring under efficient control the export and interstate commerce in opium and other habit-forming drugs. Both formally, and informally, it was pointed out to the American delegates at that conference that the other nations could have little hope for a final suppression of the opium and allied evils by international action so long as the United States, which had initiated the movement, failed to adopt the standard of national control in vogue in several European nations and in Japan."*

*The International Opium Conference. Hamilton Wright. The American Journal of International Law, vol. 7, p. 135, 1913,

It was apparently bearing in mind this situation that Mr. Porter urged the Committee to approve his bill before the International Opium Conference which had to convene in November 1924 in Geneva. Mr. Porter stated that:

> "The Resolution passed by Congress 26 February 1923, declared that the true intent and meaning of the Hague Opium convention was that production of the raw materials should be limited to strictly medicinal and scientific needs. That had always been controverted by certain nations owning colonies in the Orient. At Geneva we got them to accept our construction. The resolution passed in the last Congress is therefore the accepted construction. In November we return to Geneva with a plan to enforce the convention in accordance with this construction and interpretation."

And answering to a question of a member of the Committee as to whether the passage of the bill was an essential factor in connexion with that plan, Mr. Porter added "Yes. In case this bill is passed the United States will be in a much stronger position to urge other nations to do likewise."

A similar view was expressed by Mr. William McAdoo, Police magistrate of New York in the following statement which was conveyed to the Committee: "I am quite convinced that if the United States will distinctly prohibit the manufacture of heroin, or a similar drug under any name, other nations will follow the example or else have to tacitly admit that the drug is made for addicts and not for medicinal purposes."

* * *

Almost no testimonial was raised against the bill, except for a few letters emanating from physicians, but, as the Chairman of the Committee pointed out "none of the manufacturers has asked for a hearing, and none of them has expressed himself to me or to the clerk in opposition to the bill."

Upon conclusion of the hearings, the Committee reported unanimously in favour of the proposed legislation, and, by an Act of Congress approved 7 June 1924, (the vote in both Houses of Congress being unanimous) the importation of opium for the manufacture of heroin was prohibited in the United States.

The Analysis of Heroin

Introduction

Heroin is now by far the most important drug of addiction, at least in the Western world. In the Far East, opium itself may be more important; and in some parts of the world cannabis may claim more users, but cannabis addiction is far milder, and often only a stepping-stone to heroin.

The great advantage of heroin, from the point of view of illicit traffickers, is that it seems capable of almost unlimited dilution with other substances, while still the addict obtains from it some gratification for his desire. Nearly every small peddler who resells heroin first mixes his supply with at least an approximately equal amount of lactose or powdered sugar. As his heroin is usually highly adulterated and diluted even before he gets it, it frequently reaches the final user containing no more than five per cent of the actual alkaloid, or even sometimes as little as one per cent.

A word here as to nomenclature. "Heroin," now pronounced by most English-speaking addicts as "heroyn" (two syllables), will be used in this article for the drug as it is found in the illicit traffic and used in addiction—with all its adulterations, impurities, and dilutions. It is also to be understood that this illicit "heroin" is actually a salt of the base, namely the hydrochloride. When the name is used as a real synonym for diacetylmorphine, there is no reason to deny it the regular termination "-ine" (in most cases, including this one, pronounced as in "machine") which is applied to the names of the alkaloids and bases of the same type in English and in French. In this case the base is "heroine" and the usual salt, "heroine hydrochloride." One may still speak of somewhat impure heroine, containing small amounts of acetylcodeine and papaverine derived from the original opium, and of poorly acetylated heroine, containing more or less monoacetylmorphine and residual morphine. In this article when it is necessary to refer quite specifically to the pure substance, it will be called diacetylmorphine. It may be best to caution that these distinctions in nomenclature are not generally recognized.

Heroine is manufactured from morphine by a process of acetylation. Nowadays, the whole process is often illicit. First, the opium is either produced illicitly, or if legally produced in one of the opium-producing countries, is diverted from governmental control. Then the morphine is extracted from it in a clandestine "kitchen laboratory." Finally, the morphine is converted to heroine by a laboratory process usually involving the use of acetic anhydride and benzene. Generally the operators are not skilled chemists, and cases are known of their blowing themselves up or poisoning themselves with benzene fumes. No manufacture of heroine is lawful in the United States of America, but it is permitted in some countries under the same conditions as for other narcotics under international control. Some of the heroine on the illicit market is manufactured in legal drug factories and then diverted into illicit channels. Such heroine is distinguished by its greater purity and better acetylation; this does not mean that it is any more free from adulterants and diluents by the time it reaches the addict-consumer, but it is relatively free of acetylcodeine, papaverine, monoacetylmorphine, and morphine, which are unintentional impurities.

Purpose of Heroin Analysis

In examining a "Heroin" sample in a criminal case, the primary necessity is, of course, to identify the diacetylmorphine with complete certainty, or to identify the narcotic, whatever it may be, if the name "heroin" proves to be a misnomer. The quantitative determination of the narcotic ordinarily does not affect the criminal liability, but is usually desired by the enforcement officers. Moreover, the identification, and, when feasible, the quantitative determination of the various diluents, adulterants, and impurities that may be present, supply information that may be useful to enforcement authorities in tracing connexions in the illicit traffic, and in keeping abreast of developments in the use of narcotics. For example, the discovery of the presence of methadone in certain samples may be of interest in both ways, for methadone is one of the new synthetic analgesics which is also under international narcotics control. This discovery was recently made in New York, and also in Chicago, but the distribution of methadone-containing samples was not very wide, and it is too early to say whether these cases indicate a whole new trend in adulteration or mixing of narcotics for sale to addicts.

Classification of Other Substances

The various substances that may be found in a heroin sample, besides diacetylmorphine, may supply, in favourable cases, successive "tracers" possibly connecting up street-sellers, wholesalers, manufacturers, and finally even those who recover the morphine from the original opium.

The substances may be classified as follows:

A. DILUENTS. Generally lactose or powdered sugar, but sometimes mannitol or some other substance

may be used. Usually some diluent is added by the wholesaler or even the manufacturer; the street-seller also mixes in some diluent, often a different one. When mannitol was used, it was the first diluent, and subsequent dilutions had been made with lactose or sucrose, or both.

B. ADULTERANTS. While the diluents may also be called adulterants in the usual meaning of the term, it is convenient to distinguish the substances which are merely diluents from the drugs of more or less activity which are added either to conceal the comparative lack of real heroine, or to enhance its effect. Quinine is the most common adulterant and probably occurs in more than half the heroin samples in the United States and Canada. It is probably added, for one reason, to enhance the bitter taste of the mixture, in case the addict tries to assay the strength by tasting. It is most often added as the hydrochloride; sometimes as the sulfate. Some years ago, procaine was very commonly used. The amount of quinine usually equals or exceeds that of heroine, but the procaine was only about one-sixth to one-third the amount of the heroine, and possibly it was used chiefly for its effect as a local anaesthetic. Other adulterants that have been found are barbiturates, caffeine, acetphenetidin, methadone, and amphetamine. The adulterant is generally added by the manufacturer or the wholesaler, and thereafter mere dilution is the rule.

C. IMPURITIES OF MANUFACTURE. These include monoacetylmorphine and morphine, remaining from imperfect acetylation. The absence of such impurities may be significant of diversion from legal manufacture. Some years ago a series of samples analyzed in New York and said to be heroin coming from the eastern Mediterranean were found to contain a small percentage of calcium carbonate. This probably resulted from the manufacture, but it was impossible to say whether it was incidental or accidental, or a deliberate addition.

D. IMPURITIES OF ORIGIN. These include codeine (present as acetylcodeine after the acetylation), papaverine, meconic acid, and brown colouring matter. The absence of these substances may not mean much, but their presence proves that a rather crude process was used, not only in the manufacture and purification of the heroine, but before that, in the extraction of the morphine. Some opiums are so low in papaverine or codeine that a relatively high content of one or the other of these alkaloids may even tell something about the kind of opium used. Meconic acid can only be found in rather crude heroine. A brown heroine generally means crude manufacture, but it is possible that a brown colour is left in deliberately in some cases. Even a nearly pure diacetylmorphine hydrochloride is not a pure shining white like lactose. The brown heroine can be considerably diluted with lactose and look more like "pure heroine" than if it were shining white.

QUALITATIVE EXAMINATION

(A) FOR DIACETYLMORPHINE

Colour Tests

1. Marquis' reagent (Formaldehyde in concentrated or (6 + 1) H_2SO_4)[1]—*purple red* changing to *purple*.

2. Fröhde's reagent (Molybdate in concentrated H_2SO_4)[2]—strikes *violet*, quickly changing to strong *purplish red*, fading out to weaker brown or brownish, then developing green.

3. Mecke's (or Lafon's) reagent (Selenious acid in concentrated H_2SO_4)[3,4]—*green*, quickly *greenish blue*, changing to *blue*, slowly to bluish green with yellow-brown edge, then olivaceous green.

Comment on tests 1 to 3: These sulfuric acid reagents provide highly characteristic colour tests for the spot-plate, and most adulterants and diluents do not seriously interfere. Rarely, a sample may contain so little heroine that charring of the diluent sugar with the concentrated acid will obscure the colours. Of course in that case, a separation is necessary. Imperfect acetylation does not matter as morphine and monoacetylmorphine give the same colours. The initial colour with the hydrochloride is slightly different from that with the free alkaloid or sulfate, bluer with Fröhde's reagent and more yellow-brown with Mecke's; and this effect is increased if additional chloride is present. Chloride or hydrochloride causes some effervescence with concentrated sulfuric acid. The inexperienced analyst should compare the colours with those yielded by known diacetylmorphine hydrochloride.

4. Nitric acid—light yellow solution, gradually bright *green*.[5] Concentrated HNO_3 is usually used, but a (4 + 1) acid is somewhat better (4 parts concentrated HNO_3 mixed with 1 part H_2O).

Comment: This highly characteristic test is not very sensitive and often enough it may not be obtained on adulterated, diluted samples. Morphine gives an orange red color fading to yellow; sometimes with a little morphine present a red-orange is obtained at first and later the green of diacetylmorphine develops. Monoacetylmorphine is similar to morphine.

5. Copper test. To a little of the powder on the spot plate add several drops of water, 2 or 3 drops of 3% H_2O_2, a drop or two of NH_4OH, and stir with a piece of copper. A pink to red color is produced.

Comment: The reaction was originally discovered by Deniges; the form of the test used here was introduced by Oliver.[6,7] The test is given by various phenols and their acetyl derivatives including morphine and diacetylmorphine.[8] The stirring with copper should cause the formation of bubbles of oxygen, and in the absence of diacetylmorphine or other reactive compound the solution should gradually turn blue; if this does not occur, the peroxide solution was too weak.

Microscopic Tests

6. Platinum chloride, H_2PtCl_6. A little of the powder being examined is dissolved in a drop of water, or

better in diluted acetic acid, on the microscope slide, and a drop of the 5% reagent solution is added, then crystals are looked for under the microscope. They form gradually and are needles in rosettes, like cockleburs; they form best at a dilution near the limit of amorphous precipitation. The crystals grow larger and form blades in rosettes in the presence of acetic acid, which also diminishes the interference of quinine, and may be used up to (1 + 1) strength. (Lewis, New York Internal Revenue Laboratory.)

Comment: This test was probably originated by Putt in 1912[9]; it is the best known crystal test for diacetylmorphine, and has long been a favourite for identification. The crystals are very characteristic, but the test is much more easily spoiled by the presence of other alkaloids than either of the two following.

7. Mercuric iodide in HCl. (The solvent solution contains about 27% by volume of concentrated HCl, or 10% by weight of HCl, and is saturated with HgI_2.) This reagent is applied to a little of the dry substance on the microscope slide. The crystals are branching threads and splinter-plates.[10,11]

Comment: The test is extremely sensitive and usually succeeds even with highly adulterated samples, though since the crystals are colourless, care must be taken to distinguish them from any undissolved particles of the powder. The reagent can also be applied to the aqueous solution.

8. Gold H Bromide in (2 + 3) H_2SO_4. A drop of reagent is added to a drop of aqueous solution of the substance on the microscope slide. The crystals are fine needles, mostly scattered, but often partially in sheaves or rosettes. The interference of quinine is much diminished by the presence of acetic acid. Use a very little of the powder scattered on the slide; add a drop of 20% (or stronger) acetic acid solution; do not stir, but after a moment add a drop of the reagent.[11]

Comment: The test is extremely sensitive, and is best obtained on a very dilute solution, containing only just enough diacetylmorphine for a light amorphous precipitate when the reagent is added. Caffeine yields somewhat similar crystals with this reagent.

Other recommended microcrystal tests for diacetylmorphine can be made on the aqueous solution with 1:20 $HAuCl_4$ in (1 + 1) H_2SO_4,[11] half-saturated sodium picrate, and either Na_3PO_4 or Na_2CO_3. The last mentioned reagents precipitate the free base, which soon crystallizes.

More tests have been mentioned than are really necessary. It is considered that with good results in tests 1, 2, 3, 7, and 8, the diacetylmorphine may be considered as positively identified, without the necessity of separating it from accompanying impurities, adulterants, and diluents.

(B) FOR DILUENTS

1. Refractive indices. The best method of positively identifying at least the predominant diluent is by determining its refractive indices, using the polarizing microscope.[12,13] The ordinary lactose is the alpha hydrate, having indices of 1.517, 1.542, and 1.555. Characteristic, rather large pieces are usually seen which are roughly triangular and show bright colour bands with crossed nicols; these show the highest index lengthwise and the lowest crosswise. Many other pieces show 1.555, but few except these triangular pieces show the lowest index. Beta lactose was found in one sample examined at the Chicago Internal Revenue Laboratory; the indices are 1.542, 1.572, and 1.585.[13] Sucrose indices are 1.538, 1.565, and 1.571; the highest and lowest are easily found on bright pieces. Mannitol indices 1.520, 1.555, 1.558.[14] It occurs in rods, which uniformly show the highest index lengthwise. The lowest index can be found on a few of the brightest rods, crosswise. The middle index can be found crosswise on crystals appearing a weak gray with crossed nicols; although the crosswise index of such crystals sometimes seems to be a little less (about 1.550), with an index solution of 1.555 numerous crystals can be found with both indices nearly equal to that of the liquid. By the refractive index method mannitol can be positively identified even in small percentages in the sample.

2. Reduction with Fehling's solution. Dissolve about 20 mg (weighed—not more) of the powder in 4 to 5 cc water. Split into two parts and add 2 drops (1 + 1) HCl to one. Heat both, then add 2 cc Fehling's solution to both and heat. Hydrolyzed sucrose—complete reduction; unhydrolyzed sucrose—none. Lactose gives considerable but incomplete reduction, only a little more in the solution heated with acid than in the other.

3. Georgia and Morales test.[15] The polyhydroxy alcohols, such as mannitol and sorbitol, yield formaldehyde on oxidation, and a test for them can be made with essentially the same procedure used for methanol in distilled spirits—oxidation by permanganate, decolorization by oxalic acid in the presence of sulfuric acid, and restoration of the colour of Schiff's reagent (decolourized fuchsine solution).

(C) FOR ADULTERANTS

1. Quinine or other fluorescent compounds. A little of the powder is dissolved in dilute sulfuric acid in a test tube or on the microscope slide and observed under ultraviolet light. The General Electric 250 watt "Purple X" lamp is especially useful for such observations. Nupercaine also fluoresces strongly.

2. Herapathite crystals[16] for quinine identification. A little of the powder is treated on the microscope slide with a drop of iodine reagent C-3, and a cover glass applied. If quinine is present the herapathite crystals usually form quite readily and are easily recognizable by their properties of pleochroism, especially with the polarizing microscope. The reagent, a variant of Iodine reagent C-1,[17] and easier to make, contains: Concentrated I:KI solution (10 grams iodine plus 10 grams KI dissolved in a little water and then

diluted to 100 cc; this can be kept as a stock solution)—0.4 cc, glacial acetic acid—2.5 cc; water—2.6 cc, (1 + 3) H_2SO_4—0.5 cc. (Total 6 cc.) This reagent will keep for a week or so in a rubber bulb flask.

3. Sanchez test for procaine and other primary aromatic amines.[18,19] A solution of furfural in acetic acid, applied to the dry powder on the spot plate, yields a bright red colour with any speck of procaine or other primary aromatic amine. One part of freshly distilled furfural in 3 parts alcohol does not become badly discoloured during storage in a refrigerator and may be kept as a stock solution. One part of this solution mixed with 4 parts glacial acetic acid makes a good reagent.

4. Chromium sulfate-chloride reagent for methadone.[20] This reagent can be applied either to a drop of solution or directly to a little of the dry powder on the microscope slide, and will readily yield the methadone crystals even in the presence of much more heroine or quinine or both.

Other adulterants are less common but have been found and identified, in certain samples, in the course of quantitative examinations.

(D) FOR IMPURITIES OF MANUFACTURE.

In discussing the nitric acid test for diacetylmorphine, it has already been mentioned that this may show the presence of morphine or monoacetylmorphine by an orange colour. The following tests may also be used:

1. $FeCl_3$. To the solution on a spot-plate add 1 drop of 10% $FeCl_3$ solution. Morphine or monoacetylmorphine yields a green to blue colour, but it is not a very sensitive test. The test is due to the free phenolic hydroxyl, which is possessed by monoacetylmorphine and morphine but not by diacetylmorphine, which yields no reaction in this test.

2. Iodic acid tests. To two "spots" of the solution add a drop or two of 5% HIO_3 solution, and to one of the "spots" add 2 or 3 drops of H_2O_2 solution; then add NH_4OH to both. The one without peroxide turns dark brown (Lefort test),[21] and the one with peroxide, red.[22] These are phenolic reactions, to which morphine and monoacetylmorphine are sensitive. In diacetylmorphine the phenolic hydroxyl is acetylated, and it gives nothing, or at most a slight reaction due to partial hydrolysis.

(E) FOR IMPURITIES OF ORIGIN.

1. Ferric chloride test for meconic acid. Some of the powder is dissolved in water, the solution strongly acidified with HCl and shaken two or three times with ether. The separated ether extracts are shaken with a little dilute ferric chloride solution, which turns red if appreciable meconic acid was present.

There do not seem to be any simple tests in use for codeine (acetylcodeine) or papaverine in the presence of the other constituents of samples. These have been identified after separation in the course of quantitative determinations of the alkaloids present.

(F) FURTHER QUALITATIVE EXAMINATION.

1. Chlorides and sulfates. Test a drop of the solution of the "heroin" on the microscope slide with $AgNO_3$ solution, to confirm the presence of chlorides (the heroine seems always to be present as hydrochloride). Test another drop with $BaCl_2$ solution to see if any sulfates are present.

2. Carbonates. If any carbonate is present, the powder will effervesce with dilute acid.

3. Calcium. Treat some of the powder on the microscope slide with several drops of water and add a drop of concentrated H_2SO_4 at the side of the aqueous solution. As the liquids mix, needle crystals soon form, some of which gradually grow into highly characteristic plates.[23]

QUANTITATIVE DETERMINATIONS

The percentage of diluents is ordinarily determined merely by difference; of course allowing for the fact that the alkaloids are present as their salts, often including water of crystallization, e.g., diacetylmorphine hydrochloride $1H_2O$.

There are so many possible adulterants that it is not possible to prescribe any general method of analysis which can always be used to determine them, and methods are generally varied in accordance with the qualitative indications. In trying to make a fairly complete analysis, it is advisable first to get some measure of the total of active ingredients, consequently some methods of this nature are given first.

SOME GENERAL DETERMINATIONS:

1. Titration of amine-combined acids. Treat a weighed portion of the heroin sample, usually a gramme or two of the mixture with adulterants and diluents (preferably enough to contain approximately 0.3 to 0.4 gramme of alkaloidal salts), with 15 to 25 cc water (recently boiled); then dilute with 100 cc neutral ethanol. Titrate with n/10 NaOH, using alpha naphthol benzein indicator (0.1 to 0.2 cc of 1% alcoholic solution). In alcoholic solution, and with a suitable indicator, the salts of amines, and ammonium salts, titrate just like free acids.[24] The actual free acidity can be determined by another titration, in water, using methyl red indicator. This merely serves as a slight correction to the amine titration, unless some acidic adulterant is disclosed.

2. Titration of chlorides. This is accomplished in the usual way with standard silver nitrate solution, and potassium chromate as indicator. It may yield the total equivalent of the alkaloids, if all are present as hydrochlorides, or it may show the equivalent of the heroine in mixtures containing heroine hydrochloride and quinine sulfate. Of course neither this nor the preceding titration discloses such an adulterant as caffeine.

3. Weight of alkaloidal residue. A solution of a weighed quantity of the powder is made ammoniacal and extracted with chloroform, or if much morphine is present, with 3:1 chloroform-isopropanol. The solvent is evaporated off on the steam bath, the residue cooled and weighed. This will not include barbiturates, which have to be extracted from acid solution. In the case of a complex mixture it is advisable to acidify the aqueous solution and reextract to see what may be obtained. (See the following procedures 4 and 5.)

SOME PARTIAL SEPARATIONS:

4. Extraction of alkaloids with separation of caffeine, morphine, and barbiturates. A solution of a weighed quantity of the powder is made ammoniacal and extracted with CCl_4. The solvent is evaporated, the residue cooled and weighed. When necessary, this residue can be further examined by methods 6, 7, 8, given below. This accounts for most alkaloids, but not morphine[25] or caffeine. The aqueous solution is then acidified and extracted with $CHCl_3$. If a small portion of the extract, on being evaporated, leaves a residue, the $CHCl_3$ is shaken with dilute ammonia, then evaporated. Any residue now left is likely to be caffeine. If barbiturates were extracted from the acid solution they would be held by the ammonia, and can be recovered by again acidifying and extracting. If the qualitative tests indicated morphine, the original solution can be made ammoniacal again and extracted with chloroform-isopropanol (3:1). This prpcedure can be somewhat expanded to correspond to the following one, using CCl_4 instead of ether.

5. Ether-chloroform separation into extractive classes. This procedure is suggested for highly adulterated samples to discover what substances may be present.

(1) Treat the powder with dilute HCl and extract with ether. Shake the combined ether extracts with dilute NH_4OH, then evaporate the ethereal solution. Look for such substances as barbital or phenobarbital in the aqueous ammonia, substances such as acetphenetidin in the residue from the ether.

(2) Make the original HCl solution ammoniacal and shake out with ether. Evaporate the ether and weigh the residue. This is the main alkaloidal residue and contains the diacetylmorphine and most other alkaloids that may be present. It may have to be examined further by other methods (e.g., method 6 following; or method 7, below).

(3) Make the original solution again acid and extract with $CHCl_3$. Examine for substances such as caffeine.

(4) Make the solution again ammoniacal and extract with 3:1 chloroform-isopropanol. Examine for morphine.

MORPHINE DERIVATIVES:

6. Hydrolysis method for morphine derivatives. Often the most practicable way to determine diacetylmorphine in the presence of some other alkaloid is to hydrolyze it to morphine, which can then be separated by means of its phenolic property of solubility in alkali solution. This method can be used to determine the morphine equivalent of the total of diacetylmorphine, monoacetylmorphine, and morphine, in the usual adulterated diluted samples. As carried out by Shaffer at the U. S. Internal Revenue Laboratory at Chicago, it is as follows: Treat a weighed portion of the sample with 20 cc 1 n H_2SO_4. Reflux 1 hour (or heat in a beaker on the steam bath, replacing evaporated water occasionally). Transfer to a separatory funnel. Add 1.5 cc 1:1 NaOH. Shake out 3 times with equal volumes of $CHCl_3$ to remove alkali-insoluble alkaloids. Wash the combined $CHCl_3$ extracts once with 5 cc 2% alkali solution. Shake the main solution once more with $CHCl_3$ and shake the $CHCl_3$ with the same aqueous wash. Evaporate the $CHCl_3$ and weigh the residue, if the non-morphine alkaloids are to be determined. Combine the aqueous solutions. Add concentrated HCl to acidity and add 8 drops in excess. Add concentrated NH_4OH till basic, then 2 to 4 drops in excess. Shake three times with equal volumes of 3:1 chloroform-isopropanol. Wash the combined extracts with 1 to 2 cc water. Extract a fourth time with chloroform-isopropanol and shake the extract with the same wash water. Filter the chloroform-isopropanol extracts through a pledget of cotton into a dish or an Erlenmeyer flask. Evaporate the solvent. Dissolve the morphine residue in methanol. Titrate with n/10 H_2SO_4 until methyl red indicator begins to show red. Add boiled water and finish the titration.

DETAILED ANALYSIS:

7. Separations based on chloroform extraction from HCl solution. The following method was originally devised chiefly as a means of separating diacetylmorphine as such from quinine (without hydrolyzing the former to morphine). However, its utility goes far beyond this separation.

A. (1) Put a weighed quantity of the sample, estimated to yield not over 0.2 gramme diacetylmorphine (generally 1 to 5 grammes of the usual adulterated and diluted sample), into a separatory funnel.

(2) Treat with 5 to 15 cc cold diluted HCl (10% by volume of concentrated HCl). The larger amount is used when it is necessary to take 5 to 10 grammes of the sample because of an extremely low content of diacetylmorphine. Some undissolved lactose can be disregarded.

(3) In a second separatory, put 2 to 2.5 cc cold diluted HCl; in a third separatory, 25 cc water plus 0.5 cc concentrated NH_4OH solution; in a fourth separatory, 25 cc water.

(4) Extract 5 times, with 30 to 20 cc chloroform each time. Filter through cotton in the stem of the separatory into the second separatory.

(5) Shake each extract in turn with the wash HCl solution in the second separatory and filter into the

third separatory. Also shake each with the ammoniacal solution and filter into the fourth separatory. Also shake each extract with the wash water, and finally filter into a weighed glass dish or beaker.

(6) Finally, shake the wash HCl in separatory #2 with an additional 20 cc chloroform, and take this extract along to separatory #4, withdrawing all the chloroform from #3 and finally from #4, and filtering into the weighed dish or beaker.

(7) Evaporate the chloroformic extracts. The residue is primarily diacetylmorphine; it frequently also contains acetylcodeine, and may also contain papaverine, methadone, or caffeine. (See E.)

B. (8) Barbiturates, if present, will be in the ammoniacal solution. They may be separated by acidifying and extracting with chloroform.

C. (9) If the determination of quinine is the prime consideration at this stage, it is only necessary to combine the HCl solutions, make alkaline with NaOH, and extract the quinine with chloroform. The aqueous solution can then be reacidified, made ammoniacal, and any morphine present extracted with 3:1 chloroform-isopropanol. Such morphine is actually the morphine equivalent of the monoacetylmorphine and morphine of the original sample. Codeine, if present as such in the original sample, would be mostly left with the quinine, and extracted with it, but this very seldom occurs, as apparently the codeine is practically all acetylated in most samples. Procaine, if present, is left in the HCl solution by the extractions under A. It can be determined by method 8, below.

D. (10) For poorly acetylated samples, combine the HCl solutions after the extraction given under A, but instead of making alkaline with NaOH as in C, neutralize the acid gradually with NH_4OH while cooling, and make slightly ammoniacal. Then extract with CCl_4. This will extract the monoacetylmorphine, leaving the morphine in the aqueous layer. The morphine can then be extracted with 3:1 chloroform-isopropanol. Quinine, if present, will come out with the monoacetylmorphine, and after weighing or titrating the residue the quinine can be extracted from alkali solution, and the monoacetylmorphine (or morphine, if it has become hydrolyzed) extracted from ammoniacal solution with chloroform-isopropanol, titrated, and the titration calculated as monoacetylmorphine. Procaine, if present, would also come out in the CCl_4 in this step.

E. (11) In order to determine the various alkaloids in the residue from the chloroform extracts of procedure A, the hydrolysis method is used. When the sample has evidently been made from an impure morphine, the papaverine and codeine are of interest (the latter comes from acetylcodeine reconverted to codeine by hydrolysis), and they are separated from the morphine by shaking out the solution, after making it alkaline, with CCl_4. Methadone, if present, is separated from the morphine resulting from the hydrolysis in the same way. No detailed studies have yet been made on its separation from codeine and papaverine.

(12) In the case of codeine and papaverine, the alkaloids are recovered from the CCl_4 by shaking with dilute H_2SO_4 solution. Papaverine is then shaken out of the dilute H_2SO_4 solution with chloroform. The chloroform extracts are washed with dilute ammonia solution and water, and evaporated. The H_2SO_4 solution is then made alkaline and extracted for codeine.

(13) Usually, it is sufficient to determine the diacetylmorphine by difference, by merely subtracting the weights found for papaverine and codeine from the weight of residue found at step (7). The aqueous solution of step (12) can be reacidified, and shaken with $CHCl_3$ to remove any caffeine that may still be present (after acid hydrolysis). (To determine caffeine, however, it is better to process the original sample as in procedure 4 or 5.) The aqueous solution can then be made ammoniacal and extracted with 3:1 chloroform-isopropanol to recover the morphine, from which the original diacetylmorphine can be calculated.

PROCAINE DETERMINATION:

8. Procaine and volatile bases from alkali.[26] Usually the best way to determine procaine in heroin samples is by distillation from alkali. Procaine decomposes and a volatile amine distills over. Weigh a suitable quantity of the sample into a flask, add 150 cc water, a few pieces of granulated zinc, and 3 cc of 1:1 NaOH. Distill at least 100 cc into a measured volume of standard acid, in excess of the volatile bases, with delivery tube below the surface of the solution. Rinse the condenser and delivery tube with a little water. Titrate the excess of acid with standard alkali, using methyl red indicator. Each cc of 0.1 n acid consumed is equivalent to 0.0236 gramme of procaine or 0.0272 gramme of procaine hydrochloride. Stovaine, beta-eucaine, or pethidine will interfere, without yielding quantitative results; however, these do not seem to be normal heroin adulterants. Pethidine in small quantity can be quantitatively determined by distilling from an alkaline sodium-chloride solution. It is not decomposed by this procedure.

SOME IDENTIFICATIONS

A number of identifying reactions have already been mentioned, particularly for diacetylmorphine itself. Some others that may be necessary or useful are given here. They require separation of the substance from most of the others present.

1. *Monoacetylmorphine.* The alcoholic hydroxyl is the one acetylated; the phenolic hydroxyl is free and consequently the colour tests are practically the same as with morphine. The best microcrystal tests, which distinguish this compound easily from diacetylmorphine and morphine, are as follows:

(a) Reagent applied directly to a little of the dry substance:

(1) 1:60 $HAuCl_4$ in (1 + 1) H_2SO_4—rosettes of feathered crystals.

(2) 1:60 $HAuCl_4$ in concentrated HCl—small yellow plates, frequently triangular.

(3) Iodine reagent C-3—large red-black needles or slender rods.

(b) Reagent applied to the aqueous solution:

(4) 1:20 $HAuCl_4$ in concentrated HCl—curving branched threads in rosettes, also feathered pale yellow plates.

(5) Bouchardat No. 1 (1 gm of iodine to 1 gm KI in 100 cc solution)—branching threads in double sheaves with a bar between; dark brown and bluish-black colours.

2. *Codeine* is easily distinguished by its strong reactions with Marquis' and Mecke's reagents, along with its negative or quite feeble reaction with Fröhde's reagent. The best microcrystal test is probably the following:

(1) Iodine reagent C-3, applied to a little of the dry substance, soon yields brownish-yellow plates of characteristic appearance in shape and colour-shading, and rather dichroic with polarized light.[37]

3. *Papaverine*

(1) Fuming Fröhde's reagent gives the best colour test and one that is extremely sensitive. The colour produced is intense violet. It is convenient to keep Buckingham's reagent—10 gm ammonium molybdate in 100 cc concentrated H_2SO_4—and for "Fuming Fröhde's", dilute a portion with about 10 times as much fuming H_2SO_4 (15 to 25% free SO_3).

(2) Microcrystals: Papaverine gives a number of sensitive tests in which the crystals are small square plates, quite transparent. When they are somewhat distorted they form as 4-pointed stars. The best reagents are probably $ZnCl_2$ & HCl (reagent containing 40% concentrated HCl by volume), $HgCl_2$ & HCl (15% of concentrated HCl), and K_2ZnI_4.

4. *Procaine.* The colour test with furfural and acetic acid and the following microcrystal tests are good.[39] The reagents are added to a drop of the aqueous solution.

(1) H_2PtBr_6—with a full drop of reagent, small dark rosettes of needles form soon. If a very tiny drop of reagent is added, there is immediate crystallization in light-coloured feathered crystals.

(2) $HAuCl_4$ and HCl (25% by volume of concentrated HCl)—large irregular coarsely feathered yellow plates. Very characteristic but less sensitive than the other tests given here.

(3) $HAuBr_4$ and HCl—small orange plates, scattered and in rosettes.

5. *Caffeine.*

(1) Murexide colour test. In an evaporating dish mix a couple of milligrams of the powdered substance, a minute crystal of $KClO_3$, and 2 drops diluted HCl (1:1). Evaporate to dryness on the steam bath and continue heating several minutes longer. (If the residue remains completely colourless heat cautiously with a small flame until it becomes pinkish or brownish.) Cool and treat with 2 drops dilute NH_4OH solution. A strong purple-red colour is produced.[38]

(2) Microcrystals: 1:20 $HAuCl_4$ in concentrated HCl applied directly to a little of the dry substance—needles in sheaves and rosettes. On standing, if the concentration of caffeine is fairly high, yellow cubical grains or square-cut plates form. This test distinguishes caffeine well from theobromine and theophylline.

6. *Amphetamine*

(1) Microcrystals: 1:20 $HAuCl_4$ in (2 + 1) H_3PO_4, applied directly to a very little of the dry substance (use only about 0.1 – 0.05 mg of the pure substance). Small characteristic yellow plates or flakes soon form.

A Final Suggestion

The heroin traffic is an international one, but too little is known in any country about the characteristics of illicit heroin elsewhere. Knowledge of the adulterants found in illicit heroin in the various countries may be of value to enforcement officers everywhere. Accounts of other methods found of value for identification, determination, or particularly for detection of certain adulterants by direct tests on the heroin sample will be welcomed.

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A SCHEMATIC SEPARATION FOR USE ON COMPLEX HEROIN MIXTURES.

A SCHEMATIC SEPARATION FOR USE ON COMPLEX HEROIN MIXTURES.

This chart was prepared by Arthur Shaffer, chemist of the U. S. Treasury Department, and the procedure outlined is in use in the Chicago laboratory of the U. S. Internal Revenue Bureau's Alcohol and Tobacco Tax Division for the qualitative examination of complex mixtures sold as "heroin" in the illicit traffic.

Dissolve powdered mixture in a minimum quantity of cold H_2O, add .5 ml HCl (1 + 1) and extract quickly with pure (peroxide-free) Et_2O.

I A Remaining in Et_2O—residue on evaporation anilides and/or phenetidines, etc.

I B In dilute NH_4OH solution. Make slightly acid with HCl and extract with $CHCl_3$—residue on evaporation, test for acidic substances, barbiturates, etc.

I Et_2O extract. Shake with dilute NH_4OH (1 + 20).

Left in aqueous (dilute HCl) solution. Make ammoniacal (keeping cold) and extract quickly with pure Et_2O.

II In Et_2O. Alkaloids may be extracted directly with cold dilute HCl (1 + 9); aqueous solution then shaken with $CHCl_3$. Or, Et_2O may be evaporated and residue weighed, then dissolved in $CHCl_3$ which is shaken with cold dilute HCl.

III Left in NH_4OH layer. Make slightly acid with concentrated HCl and extract with small portions of $CHCl_3$.

III A Extracted by $CHCl_3$. Test for caffeine.

III B Left in dilute HCl. Make ammoniacal and extract with $CHCl_3$-IsoPrOH (3 + 1). Test residue on evaporation for morphine. Dilaudid possible here if present in considerable amount (see also II). If residue is too impure for definite positive test, take up in in H_2SO_4, make alkaline with NaOH (1 + 1), extract with CCl_4, saving CCl_4 for further inspection. Make aqueous layer acid with H_2SO_4 (1 + 1) then ammoniacal. Extract with Et_2O and test extract for dilaudid. Then extract with $CHCl_3$-IsoPrOH and test for morphine.

II A $CHCl_3$ extract. Wash with dilute NH_4OH (1 + 40) and then with H_2O. Evaporate $CHCl_3$ and weigh residue. Remove and test a portion to identify diacetylmorphine as such. Methadone, acetylcodeine, papaverine, etc. Reweigh remaining residue, add HCl (1 + 9) and heat one hour or more on steam bath for complete hydrolysis of diacetylmorphine to morphine (and acetylcodeine to codeine). Extract acid solution with $CHCl_3$.

II A 1 $CHCl_3$ extract. Can have methadone, papaverine, etc.

Dilute HCl solution. Make alkaline with NaOH (1 + 1) and extract with CCl_4.

II A 2 CCl_4 extract. Test residue on evaporation for codeine from acetylcodeine.

II A 3 NaOH solution. Make slightly acid with concentrated HCl or with H_2SO_4 (1 + 1) and then slightly ammoniacal. Extract with $CHCl_3$-IsoPrOH (3 + 1). Evaporate, weigh, and test residue for morphine from hydrolysis of diacetylmorphine.

II B Dilute HCl solution. Make alkaline with NaOH (1 + 1) and extract with CCl_4.

II B 1 CCl_4 extract. Evaporate. Residue may contain codeine (originally present as such), quinine, procaine, benzocaine, etc.

II B 2 Aqueous layer. Make acid with concentrated HCl or H_2SO_4 (1 + 1) and then slightly ammoniacal. Extract with pure Et_2O and wash Et_2O with dilute NH_4OH (1 + 40).

II B 2 a Et_2O extract after washing with NH_4OH. Evaporate and test for dilaudid.

II B 2 b Aqueous layer from Et_2O extraction. Add ammoniacal washes and extract with $CHCl_3$-IsoPrOH (3 + 1). Test for morphine (probably from hydrolyzed monoacetylmorphine).

Esters of Morphine

The International Opium Convention of 1912, signed at The Hague, attempted to establish control over opium, morphine, cocaine, and heroin. It was not, however, very effective. Certainly the manufacture of heroin continued to increase, and huge quantities manufactured "legitimately" were easily diverted into the illicit traffic.

After World War I the Opium Advisory Committee of the League of Nations was greatly concerned about the diversion of narcotic drugs into illicit channels. Whole countries were being debauched. In 1925 a new Convention was signed at Geneva. In some respects it represented a great advance, yet, so far as alkaloids manufactured from opium were concerned, those specifically included in the control measures were still only morphine and diacetylmorphine (heroin). Moreover, this Convention did not come into effect until 1928.

In these circumstances there sprang up a very considerable manufacture of other esters of morphine, analogous in every way to heroin, and having no medical advantages whatsoever. The other esters were in fact simply manufactured to supply narcotics for addiction. The chief one was benzoylmorphine;* another was acetylpropionylmorphine.

At the time, international control over heroin was still very weak, but was being established in the European manufacturing countries; whereas control over the manufacture of the new morphine esters in those countries was completely non-existent, and the esters also, for a time, escaped control of the national laws in some other countries, where they were distributed into the illicit traffic, or finally consumed.

Of course, some attempt had been made in the Conventions to forestall such a transparent subterfuge on the part of drug traffickers. However the slowness of countries to react when the drug use was not within their own borders made the weak provisions of the Conventions almost completely ineffective for some time.

The 1912 Convention had made its control measures applicable "To all new derivatives of morphine, of cocaine, or of their respective salts, and to every other alkaloid of opium, which may be shown by scientific research, generally recognized, to be liable to similar abuse and productive of like ill-effects." The requirement that the scientific research be "generally recognized," without any machinery provided by which this could be done, almost cancelled the significance of this provision.

Furthermore, the control measures of the 1912 Convention intended "to limit exclusively to medical and legitimate purposes the manufacture, sale, and use" of the drugs concerned (Article 9). In this Article, the word "legitimate" completely nullified the real meaning and gave some excuse for inaction. The manufacture was "legitimate" in that it was not contrary to the laws of the manufacturing country, but it loosed a flood of poison on other parts of the world.

The new Convention of 1925 was, on the point of the morphine esters, even weaker than the Convention of 1912, for it omitted any reference to "derivatives of morphine" other than the one—diacetylmorphine (heroin)—which was specifically named. Moreover, it seemed to be held by some that the 1925 Convention, when accepted, superseded that of 1912, as the following exchange will show:

(Minutes of the Eleventh Session of the Advisory Committee on Traffic in Opium and Other Dangerous Drugs, 1928, pages 36-37)

> "The Chairman recalled the well-known fact that, when a narcotic had been declared subject to the provisions of the Conventions, manufacturers hastened to manufacture another narcotic which might escape the consequences of these provisions, at any rate momentarily. Thus they had adroitly taken advantage of the fact that Article 4 of the 1925 Convention related only to morphine and its salts to put on the market a product which was not a salt of morphine but a derivative of it, and which, as such, was not under control.... The Chairman added that the question would not arise if the text of article 4 of the 1925 Convention covered, not morphine and its salts, but morphine and its derivatives. This was a question that should be examined when the Convention was submitted for revision....
>
> "Mr. Lyall pointed out that all derivatives of morphine came within the scope of the Hague Opium Convention of 1912. He was under the impression that that Convention was in force. Was he wrong?
>
> "Mr. Bourgois (France) pointed out that the obligations of the Hague Opium Convention of 1912 would still remain when the Geneva Convention of 1925 was in force in the case of those States which had not adopted the latter Convention. States which had adopted both Conventions

*Benzoylmorphine must be distinguished from benzylmorphine (Peronin). The latter is a morphine ether, and resembles codeine rather than heroin.

would continue to apply the Convention of 1912 in the case of those States which were not applying the Convention of 1925."

The provision by which the Convention of 1925 undertook to meet such a situation was its Article 10. This read as follows:

"In the event of the Health Committee of the League of Nations, after having submitted the question for advice and report to the Permanent Committee of the Office international d'Hygiene publique in Paris, finding that any narcotic drug to which the present Convention does not apply is liable to similar abuse and productive of similar ill-effects as the substances to which this Chapter of the Convention applies, the Health Committee shall inform the Council of the League accordingly and recommend that the provisions of the present Convention shall be applied to such drug.

"The Council of the League shall communicate the said recommendation to the Contracting Parties. Any contracting Party which is prepared to accept the recommendation shall notify the Secretary-General of the League, who will inform the other contracting Parties.

"The provisions of the present Convention shall thereupon apply to the substance in question as between the Contracting Parties who had accepted the recommendation referred to above."

This procedure was so cumbersome that it took at least a year and a half to reach the decision, and then it was only a recommendation, which, moreover, had to be affirmatively accepted before it had any effect. And finally, the 1925 Convention did not even take effect until 1928. Thus the decade of the 1920's came to an end before the flood of poison was stopped in all the manufacturing countries, in spite of the moral obligation which, it would seem, had already been expressed in the 1912 Hague Convention.

The situation developed rapidly after 1925: the drug manufacturers were making hay while the sun still shone. The remarks of the Chairman of the Advisory Committee of the League of Nations in 1928 have already been quoted. As a result of the discussion, and consideration of a report by Professor Knaffl-Lenz* summarizing the earlier medical and pharmacological evidence and his own observations, the Committee adopted the following resolution:

"The Committee desires to draw the attention of the Council to the attempt which has been successfully made to evade the existing system of control over the traffic in drugs by the manufacture of benzoyl-morphine and other esters of morphine which fall outside the provisions of most national laws but from which morphine can easily be recovered and which, so far as known, are liable to give rise to the same abuse; and it would urgently recommend that, pending the completion of the procedure under Article 10 of the Geneva Convention for bringing such substances within the scope of the Convention, the Governments should immediately apply to benzoyl-morphine, and possibly other similar substances if manufactured, the same control over manufacture, distribution, export and import as in the case of morphine."

Also in 1928, at its 13th session, the Health Committee of the League adopted the following resolution, designed to bring benzoylmorphine and other morphine esters under the control of the 1925 Convention:

"The Health Committee:

"Having taken note of the opinion formulated by the Permanent Committee of the Office international d'Hygiène publique on its report of May 15th, 1928;

"Having noted that dilaudide, on the one hand, and benzoylmorphine and, in general, the morphine esters, on the other hand, are capable of producing toxicomania;

"Decides to inform the Council of the League of Nations, in conformity with Article 10 of the International Opium Convention of February 19th, 1925, that dilaudide, on the one hand, and benzoylmorphine and the morphine esters generally are narcotics capable of producing harmful effects similar to those produced by products envisaged by the Convention, and that they should, in consequence, be brought within the scope of the Convention."

At its 14th session, in 1929, the Health Committee supplemented this with another resolution, which:

"Places on record that the recommendation made at its thirteenth session concerning the application of Article 10 of the International Opium Convention to 'benzoylmorphine and the morphine esters generally,' should apply to all morphine esters without exception. The possibility of exempting, in conformity with Article 8 of the Convention, those esters, the innocuous character of which may hereafter be clearly demonstrated, is, however, reserved."

At its 15th session, in 1930, the Health Committee again supplemented its previous decisions with the following resolution:

"The Health Committee,

"Consider that preparations which contain esters of morphine, di-hydro-oxycodeinone, di-hydro-codeinone (dicodide), di-hydro-morphinone (dilaudide) should be treated in the same manner as those which contain diacetylmorphine, that is

*See the second article by Dr. Knaffl-Lenz in Bulletin, No. 4, Volume IV.

to say, they should come within the scope of the Convention, whatever the percentage of narcotic substances contained may be.

"It also considers that all salts of these substances should come within the scope of the Convention according to the provisions of Article 10 of the said Convention."

This virtually completed (5 years late) the slow process of bringing the morphine esters under full control, so far as this was possible under the 1925 Convention.

What the situation was like at its height may be judged from the following excerpt from the report of the Permanent Central Opium Board on its work during its sixth and seventh sessions:

> "Large quantities of these drugs [esters of morphine] were manufactured, and as they are not, as far as is known, used for either medical or scientific purposes, they can only have been intended for the illicit traffic. The Board cannot affirm that its calculations in this matter have any claim to accuracy; but, as far as the information at its disposal allows it to form a judgment, it would seem... that some *12 tons* of morphine were manufactured in 1929 and became available for the illicit traffic in the form of esters." (Italics ours.) (C.629.M.250.1930.XI.)

In 1928 *six tons* of benzoylmorphine were sent to Dairen, destined for China. 1350 kg were seized, but over 4½ tons got through, and presumably were used by addicts. Mr. Lyall (Assessor) at the eighteenth session of the Advisory Committee on Opium and other Dangerous Drugs, while commenting on the small penalties imposed on the traffickers (page 67), remarked that "He understood that 1350 kg was equivalent to 270 million maximum medical doses of heroin. If this were so, and if, as he believed, 2700 doses were sufficient to destroy one person body and soul, the quantity in question was enough to bring destruction on 100,000 people." Actually this was the smaller of the quantities referred to, which was seized; the quantity which completely disappeared in the illicit traffic, on this one occasion, was three times as great.

An analysis by the League Secretariat of the international trade in morphine, diacetylmorphine, and cocaine, for the years 1925–1929, indicated that some *36 tons* of morphine had been made available for the illicit traffic in the form of morphine esters, or possibly in some cases other drugs not covered by the 1925 Convention. (Report to the Council, Advisory Committee on Traffic in Opium and Other Dangerous Drugs, 14th session, 1931, page 3.) These esters had no medical use and their manufacture was abandoned when controls were imposed.

Full control was imposed in Switzerland as of 1 February 1930; the conversion of morphine into drugs "not covered by the Convention" promptly dropped from 5475 kg in 1929 to 1875 kg in 1930, plus a mere 123 kg of benzoylmorphine, reported separately for the first time in that year.

The most enormous manufacture was in Germany. There the manufacturers converted the prodigious amount of 18620 kg of morphine into drugs "not covered by the Convention" in 1929. With the imposition of controls by the German Government, this amount promptly dropped to 9060 kg in 1930 and to 4060 kg in 1931, where it held fairly steady (5195 kg in 1932 and 4861 kg in 1933). These later figures represented the medical demand for codeine and ethylmorphine, the manufacture of which has been reported as 3890 kg in 1921. To the later figures would also have to be added any conversion of morphine for medical needs into dihydromorphinone, as this was only reported separately after controls were imposed; but the amount only averaged 50 kg annually from 1930 to 1933. It would appear therefore that the medical needs supplied by the German manufacturers could easily have been met by some 6 tons of morphine converted into the products in question, whereas some 18.6 tons were converted in 1929, more than twice as much, it would seem, for addiction as for medical needs.

It is seen that the outpouring of narcotics from Europe in the latter half of the 1920's resulted from several factors: reluctance in some cases to accept international obligations in the narcotics field, defects in the Conventions when strictly construed, the existence of a few utterly unscrupulous manufacturers who were ready to supply the drug traffickers, and the slowness of countries to react when the drug use was in some other part of the world.

It may be pointed out that in spite of the vastly improved provisions of the 1931 Convention for manufactured narcotics, and the 1948 Protocol for new narcotics, some similarity can be seen in the post-war world to the situation described in the preceding paragraph. The factors cited have continued to operate, to some extent and in some countries, both in regard to the manufacture of heroin and also as regards the advent of new analgesics of addicting capacity. Nothing, however, has yet approached the earlier exploitation of heroin or the morphine esters which were used as substitutes for heroin.

Heroin (Diacetylmorphine): Laboratory and Clinical Evaluation of its Effectiveness and Addiction Liability

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Heroin is "a drug with no legitimate use. Its importation, manufacture or possession is illegal. It is four to six times more powerful than morphine. No drug is more habit-forming; none has more deleterious effects." Thus did a Washington Post article on January 4, 1953, describe the drug; such seems to be the opinion generally held in the United States. Is it justified by laboratory and clinical experience?

Laboratory Evaluation

In the monograph, The Pharmacology of the Opium Alkaloids, by Krueger, Eddy and Sumwalt[1] a chapter is devoted to heroin and a very extensive bibliography, including many references to clinical experience, is appended. No useful purpose would be served by reviewing again all of the older literature; more desirable would seem to be a summary of the laboratory data on the more important aspects of the drug's action with emphasis on quantitative comparisons with morphine.

The monograph stated that "heroin is strongly narcotic and analgesic for most animals." Eddy and Howes[2] reported that the analgesic dose of heroin in the cat was 0.43 mg./kg. intramuscularly, comparable to 0.75 mg./kg. of morphine, and that both drugs produced excitement in the cat in slightly smaller dose (0.4 mg./kg. for heroin, 0.53 mg./kg. for morphine). Seevers and Pfeiffer[3] found that heroin was analgesic, sedative, and sometimes euphoric for man (normal volunteers) at a dose of 2 mg. total subcutaneously or intravenously, and that its action was more rapid in onset but of shorter duration than that of morphine. The euphoric effect of heroin exceeded that of morphine. Lasagna and Beecher[4] also gave heroin subcutaneously to a group of normal subjects in a total dose of 2 mg. Two of nine had slightly pleasant reactions, succeeded in one by an unpleasant depressed feeling. One subject considered his reaction definitely unpleasant. The chief complaint among the others was "fogginess" and difficulty in concentrating, neither pleasant nor unpleasant. Morphine, 10 mg. subcutaneously, in the same subjects, also produced predominantly a feeling of grogginess and sleepiness with jittery feelings in some instances. To only one subject was the reaction definitely pleasant; he felt relaxed, peaceful, contented and optimistic. One other subject experienced definite physical and mental relaxation with a desire merely to sit back and enjoy the relaxation.

Thorp[5] in 1946 re-assessed the analgesic effectiveness of heroin using a thermal stimulus applied to the tail of the rat. He found that 0.5 mg./kg. subcutaneously was slightly less effective than 3.5 mg./kg. of morphine and had a definitely shorter duration of action. Jackson,[6] also using a heat stimulus differently applied to the rat's tail and injecting the drugs intravenously, reported that for equal intensity of analgesic action 0.04 mg./kg. of heroin was equivalent to 2.0 mg./kg. of morphine, but that for equal duration of action the doses were 0.11 mg./kg. of heroin and 2.2 mg./kg. of morphine.

Still more recently, Herr, Nyiri and Venulet[7] reported that heroin was 8.3 times more effective than morphine when administered subcutaneously to normal rats. They compared heroin with a 4.0 mg./kg. dose of morphine, an amount which was "100 percent analgesic"; that is, increased the reaction time (tail flick response to a radiant heat stimulus) in each of a group of 10 animals to more than 2.5 times the normal reaction time of the same group. The analgesic effectiveness of heroin and of morphine was reduced in rats in which the spinal cord was transected in the dorsal region. The reduction was proportionately the same for both drugs; the 100 percent analgesic dose was 20 mg./kg. for morphine, and heroin was 7.9 times more effective than morphine in the spinal animal. This result can be taken to mean that both drugs have the same sites of action for analgesic effect, according to the authors, all sites of transmission of nociceptive stimulation, in the cord, in the thalamus, and in the cortex.

In our experience,[9] using a method of heat stimulation in mice,[9] comparable analgesic doses were 0.9 and 2.0 mg./kg. subcutaneously, and 15 to 20 and 3.9 mg./kg. orally, for heroin and morphine, respectively. The duration of action of heroin was barely half that of morphine. It is remarkable that, although heroin is more than twice as effective as morphine subcutaneously, morphine is 4 to 5 times more effective than heroin orally. The decrease in effectiveness of heroin when given orally, since heroin becomes less effective than morphine, can hardly be accounted for by prompt deacetylation. These results are on an experimental animal but they may make more understandable the large oral doses of heroin, 5 to 10 mg. and above, reported in the older clinical literature.

Dreser[10] claimed very early that heroin had a specific effect on the inspiratory phase of respiration, increasing its duration. He said that this would cause air to be drawn more deeply into the lungs and could be helpful in respiratory disease. A specific effect was not confirmed by other careful investigators; rather they have shown[11,12,13] that heroin and morphine act qualitatively alike on respiratory activity, decreasing the rate, affecting variably tidal volume and decreasing significantly minute volume. Quantitatively, however, the difference is very sharp. For example, according to Impens[14] 0.42 mg./kg. of heroin subcutaneously had as much effect on the rabbit's respiratory minute volume as 1.5 mg./kg. of morphine. Wright and Barbour[13] said that the least dose causing a decrease in respiratory activity of the unanesthetized rabbit was 0.017 to 0.035 mg./kg. of diacetylmorphine and 0.32 mg./kg. of morphine administered subcutaneously. Larger doses, 0.25 mg./kg. of heroin or 2 to 3 mg./kg. of morphine, were required to lower the rabbit's rectal temperature or slow the heart rate. Keil and Pöhls[15] reported that comparable doses for 40 to 50 percent reduction in respiratory minute volume were 0.225 and 2.8 mg./kg. for heroin and morphine, respectively. According to the last authors heroin was 12.5 times more potent as a respiratory depressant, 8 times more potent as an analgesic.

The older statements in the literature give little basis for a quantitative comparison of the effect of heroin on gastro-intestinal motility but indicate a qualitative similarity to morphine. Plant and Miller,[16] as the result of a very careful study of the action of morphine, said that it and heroin were approximately equal in potency, each increasing the tone of the intestine of the unanesthetized dog at a dose of 0.1 mg./kg., subcutaneously, or intramuscularly. Dreyer[17] indicated that heroin was twice as effective as morphine in modifying intestinal movements; but Walton[18] agreed with Plant and Miller on the quantitative similarity in the effect of heroin and morphine on the dog's intestine. In contrast to these observations, Eddy and Howes[2] observed suppression of intestinal evacuation in the rabbit with 0.7 mg./kg. of heroin and 6.0 mg./kg. or morphine. Emesis occurred less frequently with heroin than with morphine in dogs[16] and cats.[2]

Heroin is more toxic and more convulsant than morphine in various animal species. Eddy and Howes[2] recorded an average fatal dose of 262 mg./kg. and a minimal convulsant dose of 196 mg./kg., subcutaneously administered in mice. The average fatal dose for morphine was 531 mg./kg. and convulsions very rarely occurred with survival. However, for morphine and its derivatives relative toxicity for animals is not a safe criterion of probable toxicity for man. A much better basis for prediction is the degree of respiratory depression produced in an unanesthetized animal because of the very great sensitivity to opiates of man's respiratory mechanism. Heroin is at least 10 times more potent than morphine as a respiratory depressant and consequently is likely to be at least 10 times more toxic for man. Compared to this probable 10:1 toxicity ratio the greater analgesic potency of heroin is not as impressive as it first appeared. The toxicity figures are for subcutaneous injection and the quantitative data for analgesic effect by the same route of administration rate heroin as only 2 to 8 times more effective than morphine. Also all agree that the duration of action of heroin is shorter.

It is perhaps not surprising that quantitative data on the effectiveness of heroin against cough are mainly lacking, since only recently have methods been developed for the production of cough in even an approximately reproducible manner. Hillis,[19] using a single human subject and spraying irritant vapors into the larynx, compared morphine ¼ grain, heroin ¼ grain, methadone ¼ grain, codeine 1 grain and a placebo (normal saline), all given subcutaneously. All of the doses seem excessive but the author said that heroin was most effective and that codeine was no more effective than the placebo. The percent of trials with which drowsiness occurred was 86 for heroin, 68 for morphine, 69 for methadone and 43 for codeine. Beecher[20] was unable to suppress cough produced in normal human subjects by intravenous injection of small doses of paraldehyde. He tried 2.5 mg. of heroin subcutaneously, 10 mg. of codeine orally, 30 mg. of codeine intravenously and 5 mg. of morphine subcutaneously. This work is continuing with production of cough by a more "natural" method, inhalation of an irritant vapor, and extensive exploration of the usual, oral, route for antitussive medication.

Again referring to the monograph[1] the statement is made that, "Tolerance to at least some of its (heroin) effects have been seen in all of the animals studied." Two outstanding experiments have been carried out on the production of tolerance and addiction to heroin in monkeys with parallel observations on morphine. The one was by Kolb and DuMez,[21] and the other by Seevers.[22] The former made monkeys tolerant to heroin and morphine by daily subcutaneous administration. Doses attained in 8 to 10 months were 40 mg. of

heroin (12 to 13 mg./kg.) and 180 to 200 mg. of morphine (75 to 90 mg./kg.) compared to starting doses of 2 to 4 mg. of heroin and 7 to 8 mg. of morphine. The dosage increment was greater for morphine than for heroin, but because of the difference in duration of action heroin was given several times a day toward the end of the experiment, morphine never more than twice. General deterioration in health occurred, worse with morphine, and severe abstinence symptoms upon abrupt withdrawal, again worse with morphine. In previously untreated animals 7 mg. of heroin or 85 mg. of morphine might kill but the average fatal dose was not determined. Depression, manifested by drowsiness, sleep and muscular weakness, occurred sooner and was of shorter duration but was more persistent in its occurrence immediately after an injection, throughout the experiment with heroin. After surviving a single large toxic dose of either drug, animals were a little less sensitive to another dose; but after prolonged daily administration and 6 weeks to 2 months of abstinence, sensitivity to either drug was greater than at the beginning of the experiment.

Seevers also found that depression was more rapid in onset and of shorter duration in the monkey with heroin than with morphine. In animals receiving the drugs subcutaneously daily for 9 months or more the morphine dosage was increased from 10 to 125 mg./kg., the heroin dosage from 2 to 25 mg./kg. Abrupt withdrawal was followed by equally severe abstinence phenomena with either drug; the signs of abstinence appeared earlier with heroin.

Two types of experiment on the addiction liability of heroin have been performed at the U. S. Public Health Service Hospital for addicts at Lexington, Kentucky. In the first experiment[23] heroin was substituted for morphine in 9 morphine addicts. These men had been stabilized on 140–400 (average 200) mg. of morphine daily. Heroin substituted for morphine in doses ranging from 40–120 (average 71) mg. daily, or a substitution ratio of 1 mg. of heroin hydrochloride for each 3 mg. of the stabilization dose of morphine sulfate. The heroin was subsequently abruptly withdrawn and the intensity of the abstinence syndrome which followed was measured by the method of Kolb and Himmelsbach.[24] The intensity of the abstinence syndrome has been plotted in fig. 1 on the basis of hourly point scores and in fig. 2 on the basis of total daily point scores. Average figures for a large group of morphine withdrawals are plotted on each graph for comparison. The significant difference is in the rapidity of onset and subsidence of the abstinence phenomena. The plotted curve for heroin crosses the 10-point level within 5 hours and the 15-point level within 7 hours. The plotted curve for morphine does not reach the 10-point level until the 13th hour and the 15-point level until the 15th hour. Also at the 39th hour the heroin abstinence intensity is already beginning to decline while that for morphine is still rising. The difference

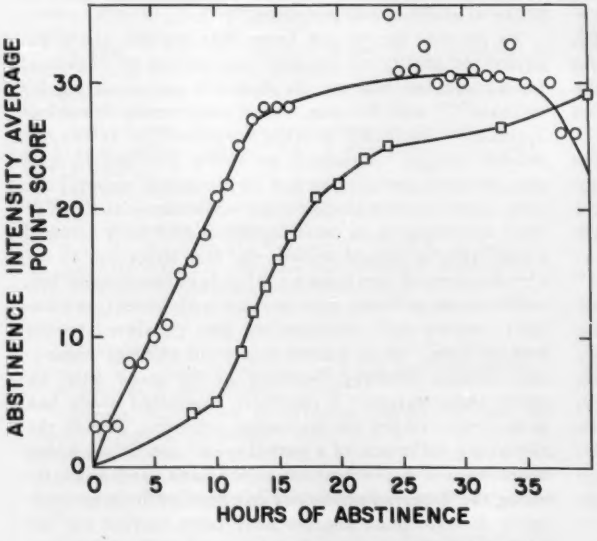

Fig. 1. Intensity of abstinence syndrome in man, hourly point score, method of Kolb and Himmelsbach.[24]
□—— □ Morphine
○—— ○ Heroin

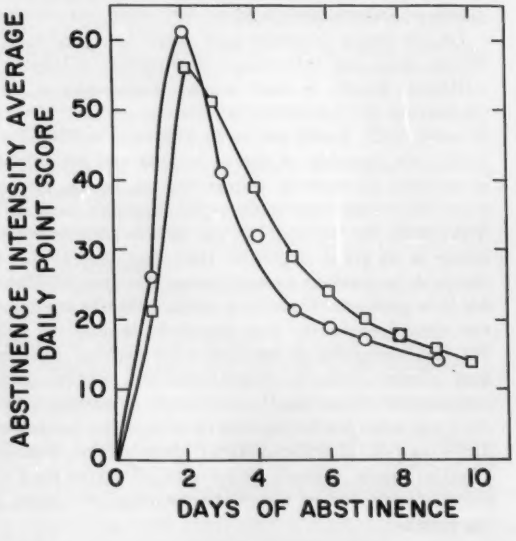

Fig. 2. Intensity of abstinence syndrome in man, daily point score, method of Kolb and Himmelsbach.[24]
□ —— □ Morphine
○ —— ○ Heroin

is not as striking in the daily point scores but again the curve for average intensity of heroin abstinence phenomena rises more rapidly, reaches a slightly higher level and subsides more rapidly than the corresponding curve for morphine.

The second experiment[25] consisted in a direct addiction study on two former addicts, free of drugs and non-tolerant when the experiment was started. The experiment was designed for a different purpose and was not ideal for a direct comparison with morphine but nevertheless confirms and extends the results of the substitution study. Both subjects received heroin subcutaneously four times a day, 15 mg./dose from 3-30-52 to 4-25-52, 30 mg./dose from 4-26-52 to 5-9-52 and 45 mg./dose from 5-10-52 to 5-20-52. Morning pre-injection abstinence phenomena (yawning, lacrimation, rhinorrhea, mydriasis) were observed as early as 4-4-52, the 6th day on the 15 mg. dose, 5-2-52, the 7th day on the 30 mg. dose and 5-14-52, the 4th day on the 45 mg. dose. Once pre-injection abstinence phenomena began, they increased in intensity until the dose was raised and concomitantly the subjects demanded such dose increase. Each time the dose was raised the pre-injection phenomena disappeared temporarily but reappeared as indicated.

After 59 days of addiction, abrupt withdrawal of the heroin was followed by very severe abstinence symptoms, reaching peak intensity from the 19th to the 28th hour and largely subsiding by the 48th hour. After completion of the experiment the subjects were not asked if they preferred heroin but both were eager to start another heroin experiment.

On the basis of above and previous experience Dr. Wikler drew the following conclusions: Milligram for milligram heroin is more potent than morphine in the production of "satisfaction" for the addict; its action is more rapid, hence produces a greater sense of well-being; the duration of action is less and pre-injection abstinence phenomena appear sooner, hence, more frequent injections and more rapid increase in dose are inevitable; the intensity of the heroin abstinence syndrome is as great or greater than that of morphine and the peak is reached sooner, hence the over-all "need" for it is greater. There is evidence that being dependent (physiologically and psychologically) on opiate drugs is attractive to the addict for various reasons—new direct sources of gratification, social esteem (successful "hustling," comparable to earning money, etc.) and also predisposition to relapse by making conditioning of pharmacological dependence possible. Finally, heroin is likely to be more addicting than morphine, conditions of a non-pharmacological nature being equal.

CLINICAL EVALUATION

Heroin was introduced into clinical medicine in 1898 and there followed a flood of reports on its potency for pain and cough particularly, minimizing the incidence of side effects and the possibility of addiction. (See (1) for partial bibliography of clinical reports.) It is interesting to note, however, that one of the earliest clinical papers gave the clue to its potential danger and sounded a note of caution. Strube[26] reported that he had given heroin in doses of 5 and 10 mg. orally to 50 patients suffering from various respiratory disorders. He noted that there were no unpleasant subjective reactions; indeed the patients liked it and continued to take the heroin pills after he ceased to prescribe or had changed them to codeine for some reason. He admitted that this might indicate the possibility of addiction.

Heroin is a potent analgesic, perhaps 3 to 5 times more potent than morphine in man, though a controlled quantitative study of dose-effect relationship against pathological pain has not been done. It is also a powerful respiratory depressant in man, perhaps 10 times more powerful than morphine, though again a controlled quantitative study of dose-effect relationship, especially of the response to equally effective analgesic doses, has not been done. The most insistent claim for its continued use, however, stems from a supposed specific effect on cough.

The dose of heroin for oral administration commonly recommended in the literature ranges up to 10 mg. This does not suggest striking or specific antitussive action if one recalls that the oral antitussive dose of codeine need not be greater than 10 mg.[27] and that it is 5–10 mg. for dihydrocodeinone.[28,29] The addiction liability of codeine is generally accepted as relatively low and that of dihydrocodeinone lies between the liability of codeine and morphine.[30]

At present we do not know that marked analgesic action or ability to depress respiration is essential for antitussive action. Evidence is accumulating for animals[31,32] and for man[33] that substances devoid of significant analgesic or other morphine-like action can relieve cough. Inasmuch as these substances with demonstrable antitussive but no analgesic action have also been shown to have no addiction liability[34,35] their development is most important and their clinical establishment should remove the last objection to the abandonment of heroin as a tool of legitimate medicine.

The claim of fewer side actions with heroin, particularly nausea and constipation, has persisted to the present time. It is based solely on clinical impression which, however, because of its mass must be given some weight. A carefully controlled study has never been carried out on normal subjects, free of the disturbing influence of a pathological condition, using morphine and a placebo for comparison, and administering the drugs as unknowns in equally effective analgesic doses. Such studies have been carried out for some of the new synthetic analgesics[36] and would seem to be the best means for quantitative estimation of side effects. Seevers and Pfeiffer[1] met partially the conditions just outlined, but their objective was not primarily assessment of side effects and they did not establish conclusively equally effective analgesic

doses. They reported for their 8 normal subjects a lower incidence of side effects and a higher frequency of pleasurable reactions when doses of 1 and 2 mg. of heroin subcutaneously were compared with doses of 8 and 10 mg. of morphine.

Any feeling about the incidence of side effects with the use of heroin is overshadowed and far outweighed by its addiction liability. On this score there can be now no question. (The monograph[1] already referred to gives many references on this point.*) Whether or not it is more liable than morphine to lead to tolerance and dependence in legitimate medical practice, it is the drug of choice in the illicit drug traffic and among a great many of the addicts which that traffic supplies, in part at least because of the small size of the effective dose, making for easier smuggling of profitable amounts, and the rapid and intense reaction which the addict experiences when the drug is given intravenously.

In conclusion one must say that any superiority for heroin has not been established by controlled quantitative data. Qualitatively it is like morphine. Any useful effects of heroin can be obtained with morphine and other morphine derivatives, some of which are certainly safer.[35, 36, 37] Besides we now have synthetic analgesics, methadone,[38, 39, 40] 1-isomethadone[41, 42, 43] and 3-hydroxy-N-methylmorphinan†[44, 45, 46] which can substitute for morphine pharmacologically. Heroin admittedly is subject to a high degree of abuse. If its deletion from the physician's armamentarium will aid in the fight against the illicit drug traffic, medical practice cannot suffer from its loss.

*See also Kaffl-Lenz, Erich ("Causes of the chronic abuse of Narcotic Drugs," *Bull. Narcotics*, 4, 1, 1952) for a brief summary of the rise in production and abuse of heroin.

†Dromoran, methorphinan, or racemorphan.

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Illicit Traffic in Heroin

I. Introduction

In spite of the fact that in 1951 "no less than fifty States reported to the World Health Organization that they had discontinued, or declared their willingness to discontinue its medical use,"[1] and that in a number of States, its manufacture has been suspended or prohibited, diacetylmorphine or heroin continues to be found in substantial quantities in the illicit traffic throughout the world, as shown in the following table:

WORLD TOTALS

Year	*Manufacture kg*	*Consumption kg*	*Seizures kg*
1936	870	853	867
1946	471*	553*	27
1947	581*	565*	106
1948	839*	657*	35
1949	523*	553*	77
1950	450	400*	80
1951	381*	412*	120

*incomplete.

The period, 1946 to 1951, is selected for review in this article as the first five-year period of supervision by the United Nations of the international control of narcotic drugs since it was transferred from the League of Nations in 1946.

The period, 1939 to 1945, that of World War II, immediately preceding this, was covered in two memoranda, namely "Review of the Illicit Traffic in Narcotic Drugs Throughout the World During the Years 1940 to 1945, inclusive, and the First Half of 1946,[2] and "World Trends of the Illicit Traffic in Narcotic Drugs During the War, 1939 to 1945."[3]

For comparison, references are made to the situation in 1936. The year 1936 has been chosen because it was two years after the 1931 Convention, which provided for the most stringent régime of control for international trade in heroin yet devised, had come into force, and about three years before World War II commenced.

The table above points up the fact that while legal manufacture of heroin is a source of supply to the illicit traffic in this drug, the rise or fall in the volume of legal manufacture is not necessarily followed by increase or decrease in amounts found in the illicit traffic. As a matter of fact, the table shows that, although the volume of legal manufacture for 1951 reached the lowest level in five years, the amounts found in the illicit traffic in the same year aggregated to the highest total during the same period. Moreover, reports from governments during the last two years indicated that, thanks to stricter measures of control over manufacture of and trade in heroin put into effect by various governments, diversions from legal into illicit channels due to thefts, robberies, forged prescriptions or laxity in respect of issuance of medical prescriptions have been reduced to the minimum. If legal manufacture no longer forms an important source of supply to the illicit traffic in heroin, an explanation of this continuing nefarious traffic and its sources of supply must be sought elsewhere.

Accordingly, an analysis is made in this article not only of the principal illicit markets throughout the world, as far as official information is available, and of the quantities involved, but also of the routes followed of the countries of origin and of the clandestine manufacture.

II. The Principal Illicit Markets

On the basis of information supplied by Governments,[4] the principal illicit markets for heroin during 1951 were: France, Greece, Italy, Turkey, Canada, United States of America, Japan, Hong Kong, Egypt, and Tunisia. Lesser amounts of heroin were seized in: United Kingdom, Mexico, and China (Formosa).

In 1936, the principal markets were China and the United States of America, although Canada, Bulgaria, Egypt, the Netherlands Indies (now Indonesia), and Hong Kong also reported seizures of heroin within their jurisdiction.

The world markets, by countries and continents, and the quantities of seizures in the post-war years compared with those of 1936, are shown in the table on page 46.

Seizures in France during the post-war years increased steadily, the largest total being that of 1951, although it amounted only to about 11% of the total of 1936.

In Greece, the amounts also increased steadily, the largest being that of 1951, although it was only about 5% of that seized in 1936.

[1] Report of the Permanent Central Opium Board to the United Nations Economic and Social Council on the Work of the Board During 1951 (E/OB/8, page 9).

[2] This memorandum was prepared by Mr. John W. Bulkley, assistant deputy commissioner, Bureau of Customs, U. S. Treasury Department, and printed in the United Nations document E/CN.7/68, pp. 3–22.

[3] A paper prepared by the Secretariat of the United Nations for the Commission on Narcotic Drugs, first session, 1946, and printed in the same document above on pages 23–36.

[4] Annual Reports on the working of the Narcotic Conventions and Seizure Reports.

COMPARATIVE TABLE OF SEIZURES

Country	1936		1946		1947		1948		1949		1950		1951	
	kg	gr.	kg	gr.	kg	gr.	kg	gr.	kg	gr.	kg	gr.	kg	gr.
Europe														
Austria	–	–	–	–	–	–	–	–	–	–	–	1	–	2
Belgium	–	–	–	–	–	–	–	–	–	15	–	–	–	–
Bulgaria	–	210	–	–	–	–	–	–	–	–	–	–	–	–
France	15	181	–	850	–	420	–	940	1	579	1	540	1	651
Germany	–	–	–	500	–	50	–	16	–	1	–	1	–	–
Greece	20	303	–	242	–	217	–	289	–	187	1	157	1	109
Italy	–	–	–	–	–	–	1	000	–	700	5	000	2	900
Turkey	10	000	–	–	–	–	1	302	2	202	24	384	57	038
United Kingdom	–	–	–	–	–	–	–	–	–	–	–	–	–	11
Yugoslavia	–	–	5	000	–	–	–	–	–	–	–	–	–	–
Total	45	694	6	592	–	687	3	547	4	684	32	083	62	711
North America														
Canada	–	214	–	530	–	285	–	437	–	958	1	572	1	970
Mexico	–	–	–	–	–	808	–	894	–	15	–	140	–	4
United States	58	629	8	897	23	186	28	194	30	123	20	742	26	896
Total	58	843	9	427	24	279	29	525	31	094	22	454	28	870
South America														
Argentina	–	18	–	–	–	–	–	–	–	–	–	–	–	–
Colombia	–	–	–	–	–	–	–	–	–	–	–	3	–	–
Total	–	18	–	–	–	–	–	–	–	–	–	3	–	–
Asia														
China	704	538	9	273	80	329	–	–	–	–	–	527	–	30
Indonesia	3	783	–	–	–	–	–	–	–	–	–	1	–	–
Japan	–	383	–	625	–	60	2	992	2	762	7	611	8	783
Hong Kong	21	918	–	4	–	–	–	–	35	000	22	390	18	427
Korea	1	141	–	–	–	–	–	–	–	–	–	–	–	–
Total	731	763	9	902	80	389	2	992	37	762	30	529	27	240
Africa														
Egypt	26	737	1	268	1	592	–	220	4	019	–	637	–	402
Tunisia	4	109	–	–	–	–	–	122	–	226	–	–	1	413
Total	30	846	1	268	1	592	–	342	4	245	–	637	1	815
Oceania														
Australia	–	–	–	–	–	–	–	–	–	6	–	–	–	–
New Zealand	–	–	–	–	–	–	–	50	–	–	–	–	–	–
Total	–	–	–	–	–	–	–	50	–	6	–	–	–	–
Grand Total														
Europe	45	694	6	592	–	687	3	547	4	684	32	083	62	711
North America	58	843	9	427	24	279	29	525	31	094	22	454	28	870
South America	–	18	–	–	–	–	–	–	–	–	–	3	–	–
Asia	731	763	9	902	80	389	2	992	37	762	30	529	27	240
Africa	30	846	1	268	1	592	–	342	4	245	–	637	1	815
Oceania	–	–	–	–	–	–	–	50	–	6	–	–	–	–
TOTAL	867	164	27	189	106	947	36	456	77	791	85	706	120	636

In Italy, the largest total for any one year was that of 1950, which was 5 kilogrammes. In 1951, it decreased to 2 kg 900 gr.

Turkey had by far the highest figure for 1951, which was 57 kg 038 gr., as compared with 1 kg 302 gr. in 1948, 2 kg 202 gr. in 1949, and 24 kg 384 gr. in 1950. The 1951 figure was almost six times that of 1936, which was 10 kilogrammes.

Seizures in Canada were made up of small quantities. The total increased steadily in the post-war years. From 530 grammes in 1946, it rose to 1 kg 970 gr. in 1951, as compared with only 214 grammes in 1936.

Seizures in Japan also increased steadily, the highest total being that of 1951.[5] In Japan the figure in 1936 was incomplete.

In Hong Kong, the largest total was that of 1949, namely, 35 kilogrammes. In 1951, it was almost 18½

[5] In 1946 the Prefectural Officials delivered to the United States Armed Forces in Japan 705 kg 290 gr. of heroin, part of which was from the Japanese Army stock and the remainder was collected by the Japanese Army in China during occupation.

kilogrammes—not far behind that of 1936, which was almost 22 kilogrammes. Heroin pills continued to be encountered in Hong Kong.

In Egypt, during the post-war years, seizures of heroin decreased. In 1951, it was only 402 grammes.

In Tunisia, the total was 1 kg 413 gr., almost one-fourth that of 1936.

By continents, it may be observed that in Europe heroin seizures increased steadily in the post-war years, that of 1951 having exceeded the total of the pre-war year of 1936.

In North America, total seizures remained almost constant and were less than those of 1936.

No information was available in respect of South America in the post-war years.

In Asia, the totals of 1947, 1949, 1950 and 1951 were all impressively large. The figures in respect of 1949 to 1951 were far from complete, as there was no information available on this subject in respect of a large part of the eastern and most populous part of the continent of Asia.

As regards the situation on a global scale, the total reported for 1951, though incomplete, must be considered large as even against the total for 1936; because out of the world total of 867 kilogrammes for 1936, Asia alone reported 731 kilogrammes. The remaining 136 kilogrammes was only 16 kilogrammes more than that of 1951 which, unlike the 1936 figure, did not include information normally available in respect of a large part of the continent of Asia.

III. Principal routes

In Turkey, the centers of illicit traffickers' activities were located in the provinces of Istanbul, Gaziantep and Ankara.

Heroin, completely prepared in finished form under the name of Bazon, was smuggled into Greece from Turkey by way of the Greek islands in the Aegean Sea. During the last three months of 1951, however, the route seemed to have changed its course away from Greece and pointed in the direction of the Western Hemisphere, the United States of America.

France, owing to her geographical situation and coastline on the Mediterranean, is a country of transit for illicit narcotic drugs, including heroin mainly from the Near East and destined to the Western Hemisphere, primarily the United States of America. One route runs from Metropolitan France to Tunisia, and another from Marseilles to Algiers, which is also used as a transit point.

In 1950, one important case involving 10 kilogrammes of heroin reported by the Government of Italy indicated a route originating in Trieste, which branched out into several routes leading to different cities throughout Italy. In 1951, heroin was found to have been smuggled by land from Nice in France to Genoa, and by air from Milan to Palermo.

Ninety per cent of narcotic seizures in Canada had to do with heroin. The route originating abroad reached Canada by way of the United States of America. The brown type of heroin in the earlier part of the post-war period came from Mexico by way of the United States.

An important route of illicit traffic in heroin, according to the Annual Report of the United States of America for 1951, extends from the mainland of China through Hong Kong and the Japanese ports to the United States.

According to the Annual Report of Japan for 1951, routes by sea and air existed between the mainland of China and Japan, passing through the northern part of Korea and Hong Kong.

Less traffic occurred on the route from Italy to the United States, since the Italian Government tightened its control over the manufacture of and trade in heroin within its borders. No traffic was reported from Mexico, the Government of the latter having also made stricter its control.

Sea route by the Mediterranean, land route across the eastern frontier through the Sinai desert and air route having been followed by traffickers in bringing into Egypt white drugs, including heroin, along with the black ones, opium and hashish. In recent years, heroin has, however, dwindled in amount in the illicit traffic in Egypt.

IV. Countries of origin

Italy has been a country of origin of heroin seized in France and the United States, although in recent years, owing to strict control exercised by the Italian Government over the manufacture and trade in this drug, the amounts from this source are greatly reduced.

Turkey is a country of origin of heroin seized in Egypt, France, Greece and the United States.

A "brown" type of heroin, which used to be frequently found in Canada, originated in Mexico. This traffic has also ceased in recent years, thanks to the strenuous efforts of the Mexican Government.

A new brand of heroin bearing the label, in Chinese characters, of "Red Lion Company" appeared in the illicit market in the United States. According to the Annual Report of the Government of the United States, this type of heroin under the Red Lion label was derived from sources located on the mainland of China.

Hong Kong and Japan, according to their annual reports, encountered heroin from the same sources.

V. Clandestine manufacture

If reduction in legal manufacture of heroin does not explain why illicit traffic in this drug has not yet substantially decreased, clandestine manufacture probably furnishes at least a partial answer.

Ever since the United Nations took over the narcotic supervisory functions from the League of Nations, reports of discoveries of clandestine factories have been received from a number of Governments.

In view of the importance of clandestine manufacture as a source of supply to the illicit heroin traffic a summary of cases recently reported follows:

1. In 1945, in the District of Darica, Vilayet of Kadjaeli, Turkey, a clandestine factory for the manufacture of heroin was found on a farm. Both the paraphernalia and heroin (400 grammes) were seized. (E/NS.1946/Summary, 3 July 1947, page 4 A)
2. In Sisli, Istanbul, Turkey, a clandestine factory for the manufacture of heroin was discovered in a private house: 120 grammes were seized. (Ibid., page 4 B)
3. In Ayazpasa, Istanbul, Turkey, another clandestine heroin factory was found in a private house (Ibid., page 4 C)
4. In April, 1945, in New York, U.S.A., the police discovered a clandestine heroin factory in an apartment house. (Ibid., page 5)
5. In December, 1946, a secret laboratory for the manufacture of heroin (and cocaine) was discovered in the residence of a textile merchant in Athens. Heroin manufactured in this clandestine laboratory was for use by addicts within the country. (Ibid., page 3)
6. In December, 1947, three clandestine factories were seized in Mexico. In one of them, 625 grammes of heroin sulphate were seized. (E/NS.1948/Summary 4, 30 October 1948, page 3)
7. In August, 1948, officers of the Greek Security Police discovered in Athens a clandestine heroin factory installed in the house of a trafficker. The equipment found on the premises proved to be exclusively used for the acetylisation of morphine base into heroin. (E/NS.1948/Summary 5, 1 February 1949, page 2)
8. In August, 1949, in Kowloon, Hong Kong, a clandestine heroin laboratory was seized. (E/NS. 1949/Summary 6, page 5)
9. In October, 1949, in Istanbul, Turkey, a clandestine heroin factory installed in the kitchen of a private residence was found. The raid "uncovered large quantities of materials, utensils, and chemicals ordinarily used in the manufacture of heroin, as well as large quantities of pure or semi-processed heroin." (Ibid.)
10. In March, 1950, at Silivri, Turkey, a clandestine heroin factory installed also in a private residence was discovered: 10 kilogrammes of heroin together with other materials and utensils were seized. (E/NS.1950/Summary 4, 15 September 1950, page 41)
11. In March, 1949, in Guadalajara, Mexico, a clandestine factory for the manufacture of opium alkaloids was seized.
12. On 23 May 1951, in Marseilles, France, a clandestine factory for the manufacture of heroin from crude morphine was seized. According to the Report of France, "...it is believed that an important source of the illicit traffic in narcotics was uncovered." The report also revealed that the equipment had been used for a fairly long time and that the accused was known to have had connexions with large-scale traffickers. (E/NS. 1951/Summary 4, page 3)
13. On 20 June 1951, a clandestine laboratory for the manufacture of heroin was seized at Konya, Turkey. The laboratory was installed in cellars of private houses surrounded by vineyards. (E/NS. 1952/Summary 1, 15 March 1952, page 4)
14. On 6 November 1951, at Emet, Turkey, another clandestine heroin laboratory was seized. (Ibid.)
15. On 18 March 1952, a clandestine laboratory for the manufacture of heroin from crude morphine was discovered in a shop, apparently used for repairing scales, at 29 rue des Envierges, Paris. According to the report of the Government of France, "the discovery of the laboratory in Paris, following the discovery of a laboratory in Marseilles last year (above), shows how easy it is to install an illicit laboratory for the purpose of converting morphine into heroin." The report concluded with the following significant sentence, "it seems that the installation of clandestine laboratories in France dated from 1951 and is a consequence of the cessation of diversions in Italy during the previous years." (E/NS.1952/Summary 3, pp. 2-3)
16. Another clandestine heroin factory was seized on 29 June 1952 at Montgeron, France. The illegal activities started even before 1952. (E/NS.1952/Summary 4, 15 September 1952, page 1)
17. On 22 July 1952, another clandestine factory for the manufacture of heroin for export to Algiers and to the United States was discovered and seized in Marseilles, France. (E/NS.1952/Summary 5, 15 November 1952, page 2)

This array of cases concerning clandestine heroin factories is, of course, far from being complete. It does, however, partially explain why illicit traffic in heroin continues to flourish in the face of reduction in legal manufacture of the drug and in spite of vigorous efforts at suppression of illicit traffic on the part of a number of governments.

The Mysterious Heroin Pills for Smoking

In the 1920's and 1930's a very peculiar use of drugs sprang up in the Far East, grew to enormous proportions, and spread to the United States and other countries, before it partially died down again. This was the use of "red pills" or "heroin pills" in lieu of smoking opium.

These pills were strange mixtures, generally containing such ingredients as heroin, caffeine, a cinchona alkaloid (quinine, cinchonine, or cinchonidine), strychnine, and aspirin or salicylic acid, mixed with starch, cane sugar or milk sugar (lactose), a delicate perfume, and a little dye to colour the pills. They were commonly coloured red or pink, but sometimes black, yellow, or simply dingy white. They were smoked, not in the usual opium pipe, but usually in a vase specially adapted to the purpose. Their effect was much disputed then, and is still highly mysterious.

It is said that the first seizure of those pills took place in Shanghai in 1921, and that at first they were taken by mouth, as a "general tonic," rather than being smoked. However, they were extensively smoked within a few years.

In 1925 a sensational article appeared in the North China Daily News (Shanghai) concerning the new pills, in which it was stated that 5,000 ounces of strychnine and 2,000 pounds of caffeine were being imported into China each month for the manufacture of so-called "anti-opium pills" containing heroin. The general formula was given as follows: Heroin hydrochloride 2 oz. 2 drachms, strychnine nitrate ½ oz., quinine sulfate 1 oz., caffeine 5 oz., milk sugar 48 oz., refined sugar 16 oz. With gum and water to "mass" this made about 10,000 pills of about 4½ to 5 grains each.

The newspaper article stated: "It is true that as an 'anti' opium pill, the new product serves its purpose. It does in most cases lead to the abandonment of opium, but for the reason that the new 'smoke' is more attractive, more potent in its effect as a stimulant, and, in its effect on the system of the smoker, more deadly." An expert estimated that "the average life of an addict to the new habit can only be about four years." This opinion was one extreme; other experts have been unable to see how the pills could have any effect at all—as will be related later.

The International Anti-Opium Association at Peking, China, called the attention of the League of Nations to the situation. It was mentioned that "(This) is not the type of morphia pill used by the average Chinese addict, who has changed from opium to morphine. The latter pill is simply a mixture of morphia and household flour, and is crude in both form and manufacture." It was shown that imports through the Customs at Shanghai amounted to 48,236 pounds of caffeine and 2,701 pounds of strychnine in 1923, and 22,234 pounds of caffeine and 1,304 pounds of strychnine in 1924—almost all supposed to have been used in the manufacture of heroin pills.

J. F. Macfarlan and Co., a British drug house, had been making large shipments of strychnine nitrate to China, but at this time, learning of the use to which it was put, discontinued all sales of both strychnine and caffeine to China.

The general formula given by the North China Daily News—and on the whole it was confirmed later by actual analyses—indicated that approximately 20,500 pounds of heroin—10¼ tons—must have been used in 1923 just to make these pills. As the seizures of heroin coming into China in 1923 had totalled nearly a ton, an illegal importation of more than 10 tons seemed quite possible. (However, in later years the proportion of heroin to caffeine in the pills was generally lower than was assumed in this calculation.)

In 1923 there was so little effective control over narcotics that this and other huge amounts of heroin escaping from control had probably been manufactured "legitimately" in Europe. After the 1925 Convention went into effect (in 1928), such diversion was rapidly reduced. The narcotics dealers, however, began to manufacture heroin illicitly in China itself (and in other countries), and the use of the "heroin pills" continued to spread.

In 1926 Dr. Knaffl-Lenz of Austria was asked to examine some of the pills for the League of Nations. He reported that they weighed about 0.25 gramme each, and contained 2.76 per cent heroin, 0.69 per cent strychnine nitrate, 1.38 per cent quinine sulfate, and 6.87 per cent caffeine, with some 66 per cent lactose and 22 per cent cane sugar. His experiments on the smokes "showed that in the combustion of smoking opium, as much as 15 per cent of the morphine contained in the opium passed into the smoke, but that in the combustion of anti-opium pills *neither* strychnine *nor* heroin *nor* quinine passes into the smoke; (but the smoke) contains up to 40 per cent of the caffeine content of the pills." (O.C.341(c)).

Dr. Knaffl-Lenz added that "The serious injury to the health of chronic smokers, said to result after a few years in death, is not on the face of it explica-

ble.... The effect of the smoke is primarily due to caffeine."

The first seizures of such pills in Hong Kong took place in 1928. These pills contained 2 milligrammes of heroin each, and were otherwise composed of lactose with caffeine and traces of strychnine; coloured pink, and about the size of a pea. It was said that they could be bought in Shanghai at the price of $14 per bag of 10,000 pills, and could be sold in Canton at $20 per bag. The retail price was said to be one cent per pill. In 1928, the seizure in Hong Kong totalled about 200,000 pills. (O.C.862).

A "pipe" for smoking these pills was described as "cleverly constructed out of a small porcelain vase, into the neck of which a bamboo tube had been inserted, a hole being drilled in the side of the vase to hold the pill."

An advertising leaflet of one of the pill manufacturers (described as the "Nan Yang Medicine Manufactory") was obtained in one of the seizures. In translation it read as follows:

> "It is hereby announced that I have studied medicine for over ten years and have spent several years of painstaking work in inventing "CHAN LENG TAN," one of the most efficacious of medicines. Its healing power is rapid and its effectiveness surpasses that of all other medicines. Since it was put on sale it has been welcomed by all classes of people and has been confidently used far and near. It is unanimously applauded and said to be the best medicine in the world. Letters and telegrams of praise have been pouring in and as a consequence the business prospers day by day.
>
> "Now, since people's honesty at the present day is not like it was in former days, and men's hearts are growing worse every day, there are numerous imitations. Among the imitators there are some who have no idea of the nature of medicine and are 'selling fish eyes as pearls,' giving the buyer no chance of distinguishing them. Such action is indeed highly to be resented. Considering that to deceive people with adulterated medicine is to injure their health, customers are earnestly requested to be careful in selecting the genuine goods so as to avoid being deceived.
>
> "In view of the above, the proprietor has specially improved the packing and added more ingredients to the preparation as from the fifth moon of the year Ting Mau (1927), in order to stamp out the imitation medicine and to extend his business. This announcement is made specially. Gentlemen, if you are in doubt, please give us a trial and you will be convinced of the truth of our words." (O.C.862).

Such concern for the customers would almost convince one of the notion, suggested in another connexion, that the illicit drug dealers mix quinine with their heroin to protect the addict from malarial infection, sometimes transmitted by use of a common needle!

In the Annual Reports of China from 1928 to 1932 there was mention of the seizure of red pills, white pills, yellow pills, heroin pills, narcotic pills, strychnine, and caffeine. The appearance of the two last in lists of seized narcotics is often not understood.

The Government of China was so occupied with more serious narcotics problems that there is not much in the Annual Reports of China about the pills. Most of the available information comes from Shanghai and Hong Kong.

The Annual Report for 1932 of the Shanghai International settlement (O.C./A.R.1932/5), called attention to "extensive addiction to so-called red pills," and said, "They are probably smoked more than prepared opium, especially among the poorer classes, who cannot afford to smoke the latter. The effect of the pills is similar to indulgence in opium, but is more harmful." The analyses showed morphine rather than heroin but this was probably due to hydrolysis of the heroin to morphine during analysis.

In 1933 a League of Nations document communicated some interesting information from Macao and Hong Kong. (O.C.1498).

The Government of Macao reported the following about the method of smoking and the effects:

> "Heroin pills are not swallowed but smoked; for this some paraphernalia is required—but it is, as the inquiries show, of a very simple and rudimentary kind.
>
> "One of the most usual methods in Macao is to employ a small china jar in which a little hole has been made of the same size as the pill. A tube, generally of bamboo, is then placed in the mouth of the jar through which the smoke passes. One pill after another is set in the hole and brought up against the flame of a small oil lamp.
>
> "The smoker, putting the tube to his lips and holding the jar in position, inhales the smoke caused by the slow combustion of the pill, until the pill is spent.
>
> "Sometimes, instead of a jar, small china flasks are employed such as are used in China to contain Chinese wine. These flasks have a spout through which the wine flows, but as this spout is either curved or slanting, the pill cannot be placed therein. The smoker therefore breaks off the spout at its base, and places the pill in the small hole remaining. He then proceeds to smoke the pill in the manner explained above.
>
> "Heroin pills produce a much more harmful effect on the physical condition of smokers than opium pills. The heroin-pill smoker's face is practically fleshless, and his strength decreases proportionately as his habit obliges him to consume an ever greater number of heroin pills.... The mental effects are practically the same as

those produced by opium. Smokers say that they feel well and happy as long as the kind of torpor produced by the narcotic lasts."

The report from Hong Kong contained the following information, which as will be noted is precisely contrary to that from Macao so far as the effect of the pills is concerned:

> "It appears that the smoking of red pills is becoming popular amongst the respectable merchant class, for three heroin divans have been discovered recently. The divans are said to charge $2 per 100 pills if sold for smoking off the premises, but a small fee only for smoking on the premises. The number of pills smoked is said to vary from 5 to 10.
>
> "The Monopoly Analyst has conducted some experiments using the proper type of pill-pipe, and drawing air through by means of a filter pump. He has found that all the heroin which is not consumed in the flame is deposited with a brown tarry sugary matter inside the vase which is used to form the bowl of the pipe, and that no traces of heroin can be found in the smoke which passes over and could enter the mouth of the smoker. In the pill-divans the inside of the vase is occasionally cleaned of this tarry matter, which is chiefly the result of the burning of the sugar of milk contained in the pills. The use the divans make of this residue is at present unknown. These pills have been given to confirmed opium smokers to smoke and they all report that they are dissatisfied with the result; it has in fact no result whatever and they say it is 'a very dull smoke' compared with opium. The smoke produced is different from that of opium, and smells of burnt sugar. Acetic acid is produced fairly freely: this would come from the decomposition of the aspirin contained in the pills; the amount produced by the decomposition of the heroin would be very small indeed. The result of the experiments is to throw a doubt on the usefulness of heroin in the pill magma. Probably only a careful and continued medical examination of an addict smoking a certain number of pills a day would reveal whether there is really any narcotic effect produced by smoking these pills."

Slightly later information was that "The usual dose at one smoking is 10 to 20 pills and a heavy smoker can smoke up to 500 in one day. The bags of 1000 cost $10.00 each in Shanghai." The Annual Report of Hong Kong for 1933 (O.C./A.R. 1933/53) stated, "In several cases smokers in opium divans were found smoking pills which, on analysis, proved to contain no substance usually classed as a narcotic. These pills, which were generally a very pale pink in colour, and more roughly made than the genuine kind, were found always to contain caffeine as their chief constituent, together with quinine, cinchonine, aspirin, or strychnine. The number of cases in which they were found being smoked in opium divans suggested the question whether caffeine was not the chief ingredient demanded by the smoker, and heroin a refinement unnecessary for the unsophisticated."

Another Hong Kong report of 1933 (O.C.1498(a)) mentioned the finding of black pills. These "had the appearance of the old-fashioned 'anti-opium pill' which was in common use many years ago, and was composed chiefly of opium dross." But these pills were found to be "ordinary heroin pills" only dyed black. This was considered unusual as "the word 'RED' has come to mean in ordinary Chinese HEROIN pills." The Annual Report of Hong Kong ,(O.C./A.R. 1933/53) also mentioned these black pills and said, "Presumably the alteration in colour was with the idea of passing them off as ordinary Chinese medical pills, many of which are black."

At this time it was also mentioned that the pills contained very imperfectly acetylated heroin, so that the narcotic content was actually, in part, unconverted morphine.

Also in 1933 the Shanghai Municipal Police reported the seizure of some 48,000 ounces of "Opium substitutes (red, grey, and white pills)" an enormous increase over 1932, when some 7,000 ounces of such pills were seized. (O.C./A.R.1933/3).

In 1934 a report from the Shanghai Municipal Council gave some details about the manufacture of pills (O.C.S.205).

> "The method of manufacture of heroin pills is comparatively simple and is usually carried out by ignorant workers under the direction of the clandestine manufacturer.... The pill mass is rolled and cut on an ordinary hand pill machine such as is used in any pharmacy and the pills are rounded by hand. They are then dried, either on trays in stands heated by a common earthenware stove or in desiccating cabinets in which are trays of quicklime.
>
> "With the exception of heroin or morphine, the other ingredients making up the pill are legally obtainable at any drug store and their sale is not restricted. Neither is there any restriction to the importation to China of caffeine, strychnine, quinine and other cinchona alkaloids.
>
> "There are a large variety of these pills in the illicit market. The best known types are the 'Tiger Brand,' the 'Fairy Horse Brand,' the 'Golden Dragon Brand,' and the 'No. 11 Brand,' but there are many others without labels. They are usually sold wholesale in packets, containing 1,000 and 10,000 pills."

The pills by this time generally contained more caffeine and less strychnine in proportion to the heroin than those of 1925; and they were usually smaller, although several different sizes were available.

Details were given of the seizure of some of the larger pill factories discovered during 1933. One, which turned out about 50,000 pills per day, manufactured three kinds: pink pills, containing heroin and scented with rose, white pills containing morphine, and black pills apparently without narcotic content. The pills also contained caffeine, quinine or other cinchona alkaloids, and a trace of strychnine, and weighed 0.07 gramme each (about 1 grain).

Another factory had been manufacturing the "Fairy Horse" brand of pills. The seizure included rose floral essence centifolia, jasmine oil, musk, red dye, powdered tragacanth, citric acid, strychnine, milk sugar, flour, and starch. Also raw opium, crude morphine, and morphine hydrochloride, although the only narcotic mentioned as contained in the pills was heroin. The usual pills were coloured uniformly throughout, but the "Fairy Horse" pills were white inside, coated bright pink. They weighed 0.065 gramme each (approximately 1 grain) and contained about 1.3 per cent of heroin, 8.0 per cent of caffeine, 2.2 per cent of quinine, and a trace of strychnine. The defendants arrested in the pill cases were all Chinese with the exception of one Japanese.

The same report mentions the seizure of two heroin factories, one of which was revealed by an explosion and resultant fire; and it is evident that at this time the heroin was locally manufactured, as well as the pills themselves.

It was also stated, "Since 1922 there has been observed a steady increase in (pill) addiction which in recent years has become prevalent to such a degree that it exceeds the smoking of opium itself. This widespread addiction is attributable to the fact that pills are comparatively much cheaper than opium. It is estimated (according to statements made by addicts) that 16 pills, which can be procured for 20 cents, have the same effect as approximately 50 cents worth of opium. Chiefly for this reason pill smoking has spread among a large section of the poorer people, many of whom were formerly addicted to the smoking of opium and are now turning to this form of vice which is more within their means."

Pill smoking in Hong Kong increased from 1934 to 1936, and continued to hold its own in spite of repressive measures up to 1939.

The Annual Report of Hong Kong for 1934 stated:

> "The Heroin Pill habit appears to be gaining ground rapidly. The 'Fierce Tiger' brand was not found so frequently as in 1933 but various local brands were popular.... (They) were usually of a lighter pink colour than the 'Fierce Tiger' pills and contained on the average one milligram of heroin per pill with the usual caffeine, cinchonine, sugar or sugar of milk, gum, and possibly strychnine. It was noticed that the pills were slightly perfumed with rose water or vanillin solution. The popular local brands were 'King of Flowers' (peony), 'Spring Waters,' 'King of Fragrance' and other adaptations of popular names.
>
> "In some cases pills were seized which contained a small proportion of morphine—smokers however stated that these latter pills were not so popular as those which contained heroin. Heroin Pill divans were discovered on many occasions. In these divans no opium was smoked and it was noteworthy that conditions in those divans were cleaner than those in opium divans; in fact, a better class of smoker appeared to frequent these divans. In other cases, divans were raided in which both Heroin Pills and Opium were available. It appears that two or three Heroin Pills are equal to one pipe of good prepared opium and the advantages claimed by smokers of these pills for the use of the pills instead of opium are:
>
> "(1) They are cleaner in handling and smoking.
> "(2) They do not pollute the breath as does opium.
> "(3) They do not cause constipation as does opium.
> "(4) The smoking operation is comparatively quick and the smoker can return to business.
>
> "The pills cost HK $0.10 for five pills to HK $0.10 for three pills."

The 1935 Annual Report for Hong Kong stated, "The traffic in diacetylmorphine pills has increased enormously. During the year, 654,233 of these pills were seized in 310 cases.... There was no direct evidence of the import and export of these pills. All indications go to show that they are manufactured in Hong Kong in small hand-type factories. These factories do not appear to remain in one building for many weeks; the pills after manufacture are immediately passed on to wholesale distributors."

It was also mentioned in some reports that heroin was seldom found when a pill factory was seized; the narcotic was evidently brought in at the last moment and the batch mixed immediately.

The Annual Report of Hong Kong for 1936 stated, "The situation as regard Diacetylmorphine (Heroin) Pills became rapidly worse in the early part of the year. It became obvious that these pills were being manufactured on a large scale in Hong Kong and special investigations were carried out with the object of attacking the actual makers. Persons found in charge of factories or engaged in the manufacture of these pills were committed for trial at the Supreme Court.... In many cases persons were found actually making the pills with the usual hand pill machines.... The only known local use of Caffeine of any considerable extent is the manufacture of the pills under discussion. If the amount (of caffeine) available for local consumption is taken as 8,000 pounds or approximately 3,600 kilos (a very low figure) this gives Caffeine content for at least 180 million pills of the type usually found.

In view of the large seizures of these pills this figure probably gives an accurate idea of the local consumption."

The narcotics cases at the Hong Kong Supreme Court in 1936 resulted in 46 persons convicted with sentences totalling 177 years. A table of seven pages was given tabulating the details in regard to seizures of pill "factories."

The Annual Report of Hong Kong for 1937 added the following information:

> "Although the traffic in Diacetylmorphine Pills did not increase in Hong Kong during the year under review it still overshadows the whole drug situation in Hong Kong. During the year 3,936,230 of these pills were seized in 405 cases, the great majority of the pills being found in pill factories. Many persons were found carrying these pills and special mention must be made of the number of young persons who were not of the lowest classes found smoking these pills in pill divans.
>
> "It was also mentioned that there had arisen a brisk trade in pills which were similar but contained no heroin. Enforcement was very rigorous and was believed to be getting the upper hand. However, the recorded caffeine imports were up to 12,768 pounds.

Again in 1938 the traffic in Heroin pills "did not increase." During the year, 2,713,181 pills were seized in 671 cases. Suppression measures were continued rigorously.

In 1939 the number of cases involving pills rose to 2196, from 891 in 1938, and 3,714,974 pills were seized. Caffeine imports were 14,340 pounds, and it was believed that at least 12,000 pounds of caffeine were intended for pill manufacture. Enormous quantities of pill ingredients were found in some cases, indicating that one factory could produce not less than 200,000 pills per day. Toward the end of the year the outbreak of war in Europe began to interfere with the supplies of pill materials.

Meanwhile in Shanghai, where the use of the pills had begun, a decline had set in. The seizures from 1933 to 1938 were as follows:

1933—48,121 ounces "opium substitutes"
1934—20,718 ounces "opium substitutes"
1935—11,479 ounces "opium substitutes"
1936— 2,668 ounces "narcotic drug pills"
1937— 462 ounces "narcotic drug pills"
1938— 799 ounces "narcotic drug pills"

The Annual Report for 1938 of the Shanghai International Settlement stated, "In former years, red pills were the chief drug of addiction among indigent Chinese owing to their cheapness compared with other types of drugs. During the year, however, addiction to red pills was practically non-existent in the Settlement, as was evidenced by the fact that, while police surveillance and suppressive measures continued unabated, there were only two addicts arrested, as against forty-eight in 1937." In fact, this figure should be compared with that of 3,496 Chinese convicted in 1934 for conducting pill smoking dens or smoking pills.

As pill smoking spread from Shanghai, pill manufacture did also, as it was a very simple procedure. The first seizures of heroin pills in the United States were in 1932. These perhaps came from China but within a few years pill factories were discovered in the United States.

Mr. Peter Valaer, who reminisced for the *Bulletin* in volume III No. 1, was the author of an article on "The Red Pill, or the Opium Substitute" in American Journal of Pharmacy 107, 199-207 (1935). Mr. Valaer distinguished two main types of pills. One type contained close to 2 per cent heroin while the other contained only a few tenths of a per cent, or even as little as 0.1 of a per cent. Pills of the latter type were a number of times declared "blanks" (containing no narcotics) by different analysts, until some experience had been gained in analysing them. There were also genuine "blanks." The pills were particularly mentioned in the Annual Report of the United States for 1936, both as being smuggled from China, and as being manufactured in the United States, particularly in Chicago. They were also discussed in the Annual Report of 1937. In 1938, however, it was said:

> "There were no large seizures of red heroin pills. In fact, the traffic in this form of drug appears to have dwindled to insignificance."

In 1941 the traffic in red heroin pills had disappeared, in the United States.

Post-war reports from Hong Kong show that there also the pill smoking habit eventually died down greatly. The 1949, 1950 and 1951 Annual Reports state that "The habit of smoking pills containing heroin still exists; but on a scale considerably less than that which existed prior to 1942." In 1950 there were 156,660 pills seized—about 2.54 kgs; in 1951 there were 36,315 pills seized, or about 0.6 kilogramme.

In retrospect considerable mystery still attaches to the heroin pills. How was such a mixture hit upon? It was said that the pills were not smoked at the start, and the conjecture has been made that they may have been originally intended for "cold pills." The content of strychnine rather than atropine is against this idea. During the years the pills were in vogue, the strychnine content declined to the vanishing point, but on the whole the formula was remarkably stable.

How much narcotic effect did the pills really have when smoked? It may be noted that there was another type of heroin smoking. In the Annual Report of the Shanghai Municipal Council for 1938, it was stated:

> "Heroin has also the advantage (over opium, to the addict) that it can be smoked in the end of a cigarette or with a mixture of tobacco in an ordinary tobacco pipe and the addict can therefore indulge in the habit without having of necessity to

resort to clandestine dens like the opium smoker of the same class."

Mr. Valaer in his article in 1935 indicated an opinion that the sublimate of caffeine from the red pills carried along some of the other drugs, including heroin. But, even if this was the case, how much effect would so little heroin have, and how explain the many pills that contained heroin indeed, but in scarcely more than traces? Many pills individually contained to start with only 1/250 grain of heroin (about ¼ mg), or even less—down to about 1/1000 grain (about 0.07 mg).

Our knowledge of the chemistry and pharmacology of smokes is extremely little. Was the narcotic use of the pills chiefly a fad? There is evidence both ways. Although it seems that the addicts must have obtained some narcotic effect from smoking the heroin pills, the fact that the use of the pills has tended to decline or even die out possibly indicates that they do not give much satisfaction to a confirmed addict.

Heroin and the International Conferences on Narcotics of 1925 and 1931

I. The 1925 Conference

Article 14 of the International Opium Convention signed at The Hague on 23 January 1912 provides that:

> "The Contracting Powers shall apply the laws and regulations respecting the manufacture, import, sale, or export of morphine, cocaine, and their respective salts:
>
> .....
>
> "(c) To heroin, its salts and preparations containing more than 0.1 per cent of heroin;"

In accordance with this provision, preparations containing 0.1 per cent or less of heroin might be bought and sold without any restrictions and supplied by chemists without a doctor's prescription.

At the very beginning of the Second Opium Conference, which met at Geneva on 17 November 1923, the United States Delegation put forward a draft Convention for consideration by the Conference. Among other suggestions, the following provision was included in the draft:

> Article 9 A
>
> "The Contracting Parties shall enact effective laws or regulations prohibiting the manufacture and distribution of heroin."

The Conference had also before it the suggestions made by the Advisory Committee on the Traffic in Opium and other Dangerous Drugs of the League of Nations, which did not propose any changes in Article 14(c) of the Hague Convention.

The Advisory Committee, however, in its report to the Council of the League of Nations relating to the Committee's Fifth session stated that:

> "With regard to heroin, the Advisory Committee, on the suggestion of the Portuguese representative, decided to recommend to the Council a resolution to the effect that Governments should be asked to transmit their views as to the possibility of the total suppression of the manufacture of heroin or, alternatively, the limitation of its manufacture to the minimum quantities recognized as necessary either for special cases or for prescriptions by specialists. The Portuguese representative supported his proposal by referring to certain authoritative opinions expressed in the medical world, which tended to show that the total suppression of the manufacture of heroin would not deprive the medical world of a necessary drug."[1]

The Conference first discussed the problem at its Thirteenth Plenary Meeting on 8 December 1924. Doctor Rupert Blue, one of the representatives of the United States at the Conference explained the reasons which impelled the Government of the United States to make its suggestion. Dr. Blue stated that although for several years the importation into the United States of heroin and other narcotic drugs had been prohibited by law, it was not until June 1923 that the United States Congress enacted legislation providing that no crude opium might be imported into the United States for the manufacture of heroin. Since no crude opium is produced in the United States, the Act effectively prohibited, so far as the United States was concerned, the manufacture and distribution of heroin. Dr. Blue then summarized briefly the hearings before the Committee on Ways and Means of the House of Representatives which preceded the adoption of this legislation.[2]

Dr. Blue ended his speech by saying that the suppression of the manufacture in the United States was, however, of little value unless the other manufacturing nations were prepared to take similar action, because the heroin abusively used in the United States was for the most part manufactured outside the United States and entered that country through illicit channels. While the Government of the United States had every desire to protect its people from the baneful influences of heroin, it was not for this reason alone that the United States Delegation was appealing to the other manufacturing countries represented at the Conference to suppress the manufacture and distribution of this most pernicious of all drugs. Drug addiction knows no barrier or limitation and what was the problem of the United States to-day will be the problem of other countries to-morrow and Dr. Blue invited the other countries to join the United States in a common cause against a common enemy.

At the proposal of Mr. de Myttenaere, delegate of Belgium, the Conference decided to refer the question of heroin to the Sub-Committee F of the Conference, composed of experts of the medical and pharmaceutical profession.

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[1] A. 13 1923 XI [O.C. 144 (1)] League of Nations publication.

[2] See article entitled, "The United States bars the manufacture of heroin" in the present issue of the Bulletin.

The Sub-Committee F on 28 January 1924 adopted a report in which it expressed itself as follows concerning the question of heroin.

> "The Sub-Committee decided unanimously, with the abstention of the United States of America, that it was not competent to suppress this alkaloid. Only on the recommendation of a medical enquiry throughout the whole world could its entire suppression be decided upon. Nevertheless, impressed by the terrible ravages of the heroin habit, especially in the United States of America, the Sub-Committee, in contrast to the stipulations of the previous article as regards morphine and cocaine, adopted the suppression of the percentage, which means in practice, that it is impossible to sell to the public any preparation containing even the smallest quantity of heroin without a medical prescription.
>
> "For this reason, some of the delegates found it necessary to observe that they were not empowered to accept this modification and that, although they associated themselves personally with the high motives which inspired the change, they made a reservation regarding the Government's acceptance of this suppression of the tolerance extended to other narcotic alkaloids.
>
> "At the same time, many of the delegates considered that it would be well to proceed, first, to the reduction, and then, no doubt, to the removal of heroin from therapeutics throughout the world.
>
> "With regard to the wording of the paragraph, the German delegate justly observed that the word 'heroin' could not stand by itself in the text of the Convention, since it was the property of the commercial firm and had not come into public use; it was therefore desirable to refer to this product by its chemical name of *diacetylmorphine*, putting in brackets the names (diamorphine, heroin) by which it is still known in commerce."

The United States member of Sub-Committee F, who, as indicated above abstained from giving his approval to the report, presented on this matter a minority report which read as follows:

> "It is recommended that an article providing for the suppression of the manufacture of heroin be included in the Convention (see Article 9 A of the suggestions of the United States).
>
> "The United States delegation has noted with interest the recommendations submitted by the Sub-Committee regarding the limitation of the use of heroin and would respectfully urge the Conference to take advantage of the present opportunity to place a ban upon this noxious drug in the manner indicated in Document O.D.C./C.R./13[3]. In further support of the proposal to suppress the manufacture of heroin, reference may be made to the report of the Health Section of the League of Nations:
>
> "Diacetyl-morphine (heroin) is a very dangerous drug, still more toxic than morphine and still more dangerous as regards the forming of the drug habit. Since the pharmacologists and clinical practitioners admit that heroin can be dispensed with in therapeutics, the Mixed Sub-Committee recommends the possibility of entirely forbidding its manufacture should be considered."
>
> "The foregoing statement not only constitutes a strong endorsement of the views entertained by the delegation of the United States regarding the suppression of the manufacture of heroin but would also seem to afford the answer to the statement that sufficient evidence has not been obtained to warrant the suppression of the manufacture of the drug at the present time."

The report of Sub-Committee F was discussed at the Thirtieth Plenary Meeting of the Conference on 12 February 1924, six days after the United States had withdrawn from the Conference. Professor Perrot, Delegate of France, stated that there was no reason why the Conference should deal more severely with heroin than with morphine and cocaine or why the Conference should draw up draconian measures for the complete suppression of heroin, which is a very active product of preparations which do not give rise to toxicomania. On behalf of the French Delegation, Professor Perrot requested, therefore, that heroin should continue to be dealt with as in the Hague Convention.

In the discussion which followed, Mr. de Myttenaere from Belgium and Dr. Carrière from Switzerland, the former a member and the latter the chairman of the Sub-Committee, vigorously defended its report and requested the Conference to reject the French proposal. In the absence of the United States Delegation no formal request was made for the complete suppression of heroin, but the Delegates of Poland, Dr. Chodzko, of Brazil, Dr. Pernambuco and Dr. Gotuzzo, and of Canada Dr. Riddell, pointed out that, although they were in favour of the suppression, they accepted the Sub-Committee's report as a practical measure since it appeared that the majority of the members of the Conference would not agree to it.

The Egyptian Delegate, however, expressed the view that the Health Committee of the League of Nations should be asked to carry out the necessary enquiries among international scientific institutions with a view to making it possible to suppress heroin entirely, if the enquiries proved conclusive in this respect. He proposed to insert in the Convention a clause to the effect that complete suppression would be admitted on the recommendation of the *Office international d'hygiène publique* and the Health Committee of the League of Nations. The Chairman of the Conference ruled that the Egyptian proposal should be

[3] This document contained the minutes of the Thirteenth Meeting of the Conference the gist of which has been given above.

referred to the Drafting Committee for insertion in the Final Act. The ruling of the Chairman was accepted by the Conference but the matter did not develop further and no provision was included in the Final Act.

Doctor Belances, Delegate of the Dominican Republic proposed a solution which he thought was half way between the Sub-Committee's proposal and the amendment of the French Delegation namely: that the Conference should not forbid the manufacture of heroin but should reduce the quantity proposed by the French Delegation. The Delegate of France immediately accepted a reduction by 50 per cent, i.e., to have the percentage fixed at half of the percentage stipulated in the Hague Convention i.e., at 0.05. A neutral position was taken by Sir Malcolm Delevingne who thought that not sufficient evidence has been produced before the Conference in favour of any solutions proposed. He stressed the difficulty of governments to require any change in national legislation unless strong reasons were put before Parliament.

The matter then came to the vote. Six delegations voted in favour of maintaining the provision of the Hague Convention as amended by the proposal of the Delegate of the Dominican Republic. The Conference decided then, by 21 votes, to adopt the conclusions of the report of Sub-Committee F.

II. The 1931 Conference

No special provision regarding heroin was included in the draft prepared by the Advisory Committee on Traffic in Opium and Other Dangerous Drugs for the Conference for the limitation of the manufacture of Narcotic Drugs which met at Geneva on 27 May 1931. But very early in the general debate, on 29 May, the Austrian Delegation proposed the total suppression of heroin.

The Austrian Government was of opinion that the total suppression of the manufacture of diacetylmorphine would be the most effective step in the campaign against the abuse of narcotic drugs. Heroin was the most poisonous of all the derivatives of morphine; consequently, owing to its small bulk, it was most suitable for the illicit traffic. Further, it was the only derivative of morphine which could be taken as snuff. It was therefore easier and more convenient to use than morphine. The fact that the consumption of heroin was small in many of the countries where general civilization and health organizations were most highly developed, and that its use had been prohibited in the United States of America since 1925 showed that this narcotic drug could be dispensed with, without depriving patients of medical treatment, and that heroin could be replaced by other less dangerous derivatives of morphine.

At the tenth plenary meeting, on 3 June, the Austrian Delegation proposed to include in the Convention the following provision: "The manufacture of diacetylmorphine is forbidden," and asked that this proposal should be referred to the Technical Committee of the Conference. The Polish delegate, Dr. Chodzko, warmly supported the Austrian proposal, but pointed out that it was a very radical suggestion and that, therefore, it might encounter resistance and finally be defeated, because certain countries thought it absolutely essential to have a certain quantity of heroin available for certain special cases. If any country was ready to run the risk of employing heroin, that was its own affair, but all possibility of exposing other countries should be avoided. He, therefore, proposed that heroin should in no case be exported.

The British Delegate opposed both the Austrian and the Polish proposals and asked for an immediate vote. Dr. Vasconcellos from Portugal requested the Austrian Delegation to withdraw its amendment. Other delegations, however, warmly supported the Austrian proposal as did Dr. Wu Lieu-Toh from China and Mr. Figueredo-Lora from Costa-Rica. Mr. Cavazzoni from Italy, stressing the humanitarian aspect of the problem gave his preference to the Austrian proposal but was in favour of referring both proposals to the Technical Committee. Colonel Sharman, Delegate of Canada, said that if the Austrian proposal were referred to the Technical Committee, the latter's report would be of great value in enabling the Canadian Delegation to bring to the attention of its Government and medical profession the considered opinion of so authoritative a body of experts, and thus materially co-ordinate the views held in Canada on the subject. He was not, however, in the position to commit at the present time his Government to the abolition of heroin. The Conference finally agreed to refer both proposals to the Technical Committee.

The Technical Committee at its second meeting on 8 June in its turn referred the problem to its Committee of experts composed of highly qualified specialists: Professor W. E. Dixon (British), Professor Erich von Knaffl-Lenz (Austrian),[4] Professor M. Tiffeneau (French) and Dr. P. Wolff (German). Dr. Small from the United States was added to the body.

The Committee of experts had to answer a series of questions put to it by the Technical Committee and its findings could be summarized in the following way:

Heroin is more powerful than morphine and its dose is smaller. Unlike morphine, it may be readily taken as snuff. In the East it is occasionally smoked. Also, in view of the smallness of its dose, trafficking is easier. Heroin euphoria is much more pronounced than that of morphine, and constipation does not occur in the addict.

Heroin is at least equal to morphine in its effect in the relief of pain. The experts, however, expressed the belief that the properties of heroin which render it popular with some physicians can in most, if not all, cases be efficiently replaced by other morphine drugs.

The experts further stated that in their opinion the dangerous nature of heroin from the social point of

[4] For Professor Erich von Knaffl-Lenz's personal recollections on the work of the 1931 Conference, see *Bulletin on Narcotic Drugs*, Vol. IV, No. 4.

view overshadowed its therapeutic importance. They admitted however that the opinion of the medical profession on the therapeutical value of heroin varied, not only in different countries, but even in the same country. Their final conclusion was that in view of the evidence which they possessed and especially the fact that all the beneficial actions of heroin could, in their opinion, be obtained by other less dangerous drugs, heroin could be entirely dispensed with.

The findings of the experts came for discussion at the seventh meeting of the Technical Committee on 17 June, Dr. P. Wolff and Dr. Dixon defending eloquently and highly competently the conclusions of the experts. The Committee after a lengthy debate during which the thesis advanced during the general debate were repeated with slight variations divided evenly when it came to a vote: 9 members of the Committee voted for the Austrian proposal, 9 against and 7 members were absent. According to the League of Nations procedure the Austrian proposal was considered as rejected.

The Conference considered then at its Eighteenth Plenary Meeting a draft article based on the Polish proposal which with some amendments became article 10 of the 1931 Convention.[5]

At its Thirty-Fifth Meeting on 12 July, the Conference approved Resolution VI which took place in the Final Act of the Conference and which reads as follows:

VI.

The Conference:

Recognising the highly dangerous character of diacetylmorphine as a drug of addiction and the possibility in most, if not all, cases of replacing it by other drugs of a less dangerous character:

Recommends that each Government should examine in conjunction with the medical profession the possibility of abolishing or restricting its use, and should communicate the results of such examination to the Secretary-General of the League of Nations.

[5]See article entitled, "Article 10 of the 1931 Convention."

Article 10 of the 1931 Convention

In connexion with a special issue of the Bulletin on Heroin, the editors deem it useful to give an extract of the historical and technical study prepared by the Secretariat of the League of Nations on the Convention for limiting the manufacture and regulating the distribution of narcotic drugs of July 13th, 1931, relating to Article 10 of this Convention.

ARTICLE 10.

1. *The high Contracting Parties shall prohibit the export from their territories of diacetylmorphine, its salts and preparations containing diacetylmorphine or its salts.*

(For the discussions in the Conference on Article 10, see Conference, Vol. I, pages 86-95, 139-143, 241-243; Vol. II, pages 79-80 and 93-105).

General and historical Note

By Article 10, the Convention provides a special régime for the export and import of diacetylmorphine.

Under the convention, the degree of limitation and regulation varies according to two criteria: the first is the degree of danger presented by a particular drug, and the second is the extent to which the drug is used by the medical profession. From these points of view, the drugs covered by the Convention fall into three groups:

(1) Drugs in Group II, codeine and dionine, are subjected to the least stringent measures, their manufacture being limited less strictly and their distribution being somewhat freer than in the case of the other drugs;

(2) The main body of drugs are subjected to the general scheme of limitation of manufacture and regulation of distribution;

(3) Diacetylmorphine, on the other hand, whilst treated like the main body of drugs as regards limitation of manufacture, is subjected to a specially stringent régime as regards its exports to and distribution in countries which do not themselves manufacture the drug.

The reason for subjecting diacetylmorphine to the most stringent régime provided by the Convention is that it is generally regarded as the most dangerous of the opium derivatives. It is the only derivative of morphine which is known to be absorbed by sniffing and it is extremely toxic as compared with other opium derivatives. Its therapeutic value, moreover, was regarded by a number of delegations represented at the Conference as doubtful.[1]

It was for this reason that a proposal for the total abolition of heroin was made as early as 1923 in the Opium Advisory Committee, which in its fifth session asked "the Council to request the Governments to communicate their views as to the possibility of a total suppression of the manufacture of heroin or of its limitation to the minimum required."[2] The replies received from Governments indicated a division of opinion, which continues to the present day, between Governments which were willing to consider the possibility of abolition and those which took the view that heroin is indispensable in certain cases in medical practice. A definite proposal for the abolition of the use of the drug was made and rejected at the Second Opium Conference in 1925,[3] but the Conference agreed to abolish the exemption in the Hague Convention 1912 for preparations containing not more than 0.1% of the drug.

In the Limitation Conference, a proposal was first moved to abolish the use of heroin completely. This was objected to on the grounds that the drug was of medical value; that, of the supplies which were being exported from the manufacturing countries on the basis of import certificates, practically nothing was now escaping into the illicit traffic, and that even if heroin were abolished it could be manufactured from morphine by any trafficker without special difficulty.

In view of these objections, the proposal contained in Article 10 was moved as a compromise.

§102. "SHALL PROHIBIT".

The general effect of the article as a whole is that the export of heroin is prohibited in all cases except as follows: a country which manufactures heroin may export to a non-manufacturing country, under the conditions specified in paragraph 2, the quantities required in that country for its medical and scientific needs. It follows from this that a non-manufacturing country or territory cannot export heroin to any other country or territory, as it can only obtain the supplies of heroin necessary for its own medical and scientific needs, and these supplies, as indicated in paragraph 3, are for distribution in the country itself. The pro-

[1] For the views of the experts attached to the Conference on the medical value of diacetylmorphine, see Conference, Vol. II, page 129.

[2] Document A. 13.1923.XI.

[3] Records of the Second Opium Conference, Vol. I, page 496.

hibition even applies as between territories belonging to the same country or between one manufacturing country and another manufacturing country.

ARTICLE 10, PARAGRAPH 2.

2. *Nevertheless, on the receipt of a request from the Government of any country in which diacetylmorphine is not manufactured, any High Contracting Party may authorize the export to that country of such quantities of diacetylmorphine, its salts, and preparations containing diacetylmorphine or its salts, as are necessary for the medical and scientific needs of that country, provided that the request is accompanied by an import certificate and is consigned to the Government Department indicated in the certificate.*

§103. "ON THE RECEIPT OF A REQUEST".

It was clearly understood at first that a special request from the Government of the importing country had to be addressed to the Government of the exporting country. The matter came before the Advisory Committee at its twentieth session, which referred to the matter in the following passage in its report:[4]

> "The main question submitted to the Committee was whether the provisions of paragraph 2 of Article 10, in accordance with which no contracting party may authorize the export of diacetylmorphine except 'on the receipt of a request from the Government of any country in which diacetylmorphine is not manufactured,' necessarily involved a special request *from one Government to another*, and whether, for instance, the import certificate furnished by the Government could not take its place.
>
> "The Advisory Committee considers that, if the stipulations of the Model Code[5] are strictly observed, the question settles itself. This is in accordance with the text of the Conventions, which provides that the contracting party, before authorizing export, shall receive a request to that effect, from the Government of the importing country and that this request must be accompanied by an import certificate. Moreover, the drug must be consigned to the Government Department indicated in the certificate; it cannot be consigned to a private firm.
>
> "The Committee finally adopted the following resolution:
>
> "'The Advisory Committee:
>
> "'Notes the efforts made by the countries which export diacetylmorphine to apply the provisions of Article 10 of the Limitation Convention of 1931:
>
> "'Observes that an exporting country cannot carry out the provisions of paragraph 2 of Article 10 of the Convention unless the Government of the importing country carries out its obligation under that article of making a formal request asking that the export should be permitted, and of forwarding to the Government of the exporting country this request, together with an import certificate in which the Government Department to which the drugs should be consigned is clearly designated;
>
> "'Requests the Secretariat to write to the Governments of all countries importing or exporting diacetylmorphine, drawing their attention to the terms of the above-mentioned article.'"[6]

§104. "FROM THE GOVERNMENT OF ANY COUNTRY IN WHICH DIACETYLMORPHINE IS NOT MANUFACTURED".

This rules out any export to or import by a country which manufactures diacetylmorphine—in other words, no export or import of diacetylmorphine is possible between manufacturing countries.

The Government of the exporting country must, as the Model Code (*ad* Article 10) indicates,[7] take the necessary precautions to satisfy itself that the importing country which makes the request is, in fact, a country which does not manufacture the drug. For this purpose, as the Code points out, it may consult the information received by the Secretary-General under Article 20 and the reports to the Council of the Permanent Central Board. It should also consult the list of licenced factories periodically issued by the Secretariat of the League of Nations.

Moreover, the conditions under which diacetylmorphine can be received and utilised by the importing country would even seem to preclude imports in a case where the country, whilst not manufacturing diacetylmorphine, proposed to use the imported drug for the purpose of conversion into some other drug, such as morphine or codeine. This interpretation is in accordance with the whole purpose of the article, which was to restrict export and import to the narrowest limits—i.e., to forbid all export or import of diacetylmorphine,

[4] See document C. 253.M.125.1935.XI, page 11. See also, for previous references to the matter, Report of the Committee on the Work of its Nineteenth Session, document C.530.M.241.1934.XI, pages 8–9, and Minutes of the Nineteenth Session, document C.33.M.14.1935.XI, pages 82, 85–86.

[5] The reference is to the following paragraph from the Model Code, *ad* Article 10, page 6:

"Under the terms of paragraph 2 of this article, export authorisations are to be issued only against import certificates authorizing import by a Government Department. Moreover, such import certificate is required to be accompanied by a formal request from the Government of the importing country, asking that the export should be permitted. The drug, when exported, is required to be consigned to the Government Department of the importing country indicated in the import certificate."

It should be noted that the article itself and the above passage from the report of the Advisory Committee say that the request must be accompanied by an import certificate.

[6] A circular letter to this effect was sent to Governments.

[7] Model Code, page 6.

except export by a manufacturing country to a non-manufacturing country for use as such for medical or scientific purposes in the latter country under the stringent conditions specified in the article, and those supplies as indicated in paragraph 3 are for distribution in the country of import itself.

It follows that the use of any part of the supplies so imported for re-export[8] is precluded.

In practice, non-parties must comply too with the provisions of paragraph 2 of the article, if they wish to import diacetylmorphine from a contracting party.

§105. "AS ARE NECESSARY FOR THE MEDICAL AND SCIENTIFIC NEEDS OF THAT COUNTRY".

(Compare the wording used in paragraph 1 of Article 4 and paragraph 2(a) of Article 5).

Amounts which may be imported are determined by the estimates of the importing country, subject to the provisions of paragraph 2 of Article 12 and of paragraphs 1 and 2 of Article 14.

§106. "PROVIDED THAT THE REQUEST IS ACCOMPANIED BY AN IMPORT CERTIFICATE AND IS CONSIGNED TO THE GOVERNMENT DEPARTMENT".

The drafting of this clause is defective, the words "the quantity so exported" having been inadvertently omitted before the words "is consigned."[9] The attention of Governments was drawn to the matter by circular letter, and they were asked to state whether they agreed with interpretation. Governments have since accepted the interpretation.

The stipulation that the export must be consigned to a Government Department is absolute. It cannot be made, for example, to a private firm designated by the Government.[10]

ARTICLE 10, PARAGRAPH 3.

3. *Any quantities so imported shall be distributed by and on the responsibility of the Government of the importing country.*

§107. "BY AND ON THE RESPONSIBILITY OF THE GOVERNMENT OF THE IMPORTING COUNTRY".

The Model Code *ad* Article 10 contains the following comment on this paragraph:[11]

> "Under the terms of paragraph 3 of this article, the drug imported by the Government Department concerned may be distributed by that Department, on its responsibility, either directly to doctors or pharmacists, or through authorised wholesalers."

As the Records of the Conference show, there can be no doubt that this interpretation, whereby distribution may take place by the Government Department either directly to doctors or pharmacists, or through authorised wholesalers, is in accordance with the intention of the Conference. The paragraph was, in fact, only adopted on the express understanding—as authoritatively stated by the President himself on behalf of the Conference—that the paragraph meant "that the State would be responsible for designating a competent authority to receive supplies of the drug and to distribute them, but that it would not necessarily undertake the commercial operations of selling and buying."[12]

[8] See also, as to re-export, Conference, Vol. I, pages 141, 143 and 173.

[9] See Report of the Opium Advisory Committee to the Council on the Work of the Seventeenth Session (document C.642.M.305.1933.XI, page 4). The replies received from Governments accepting this interpretation are contained in the progress report annexed to the Minutes of the Twentieth Session of the Advisory Committee (document C.277.M.144. 1935.XI, pages 107-108). That this interpretation corresponds to the intention of the Conference is shown by the original text of the article as proposed by the Technical Committee of the Conference (Conference, Vol. I, page 336).

[10] See also Conference, Vol. I, pages 139-140.

[11] Page 6.

[12] Conference, Vol. I, page 141; see also Vol. I, pages 139, 140, 142, 241, and 242.

Bibliography

HEROIN

The Bulletin on Narcotics presents a bibliography on heroin: the editors tried to make it as complete as possible and they are specially indebted to Hugo Krueger, Nathan B. Eddy and Margaret Sumwalt for their paper entitled *The Pharmacology of the Opium Alkaloids* published as Supplement No. 165 to the Public Health Reports by the United States Public Health Services.

However, due to circumstances, this bibliography is by no means final and it is hoped that readers will help to make it more complete: a supplement of the bibliography will be published in a future issue of the Bulletin when enough material has been gathered for that purpose.

Due to the nature of the sources available to the Secretariat, several of the titles are given in translation only; in that case, they are marked by an asterisk.

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